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ENDOMETRIOSIS OF THE LUNGS

Experimental Production of Endometrial Transplants in the Lungs of Rabbits

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FOR several years the senior author (7) has stated repeatedly that he surmised fragments of endometrial tissue were transported through the lymphatics and venous channels to the lungs, became embedded there and grew. This idea seems logical in view of several known facts.

In the first place, experimental autotransplantation of endometrial tissue has been made to various structures such as ovaries, tubes, abdominal wall, cornea of the eye, etc. Inadvertently during laparotomies, endometrial tissue has been transplanted to the uterine wall, tubal stump, and abdominal wall. Furthermore, Jacobson and others have shown that fragments of menstruating endometrium can be autotransplanted, thus showing the viability of mucosal tissue cast off at menstruation. It seems to be the consensus now, that Sampson's (5) theory of regurgitation of menstrual blood through the tube is responsible for the major source of pelvic endometriosis. Fragments of mucosa become implanted on the ovaries and form chocolate cysts which may rupture and further disseminate endometrial tissue throughout the lower abdomen. The diversity of structures in which endometrial tissue has been found, namely, vulva, vagina, inguinal region, uterus, tubes, ovaries, rectovaginal septum, intestinal tract, umbilicus, laparotomy scars, thighs, etc., would indicate that the lungs do not have any special resistance to the growth of this tissue. In the second place, Sampson (6), Halban, and others have demonstrated the presence of uterine mucosa in veins and lymphatic vessels. This is the logical, though not the only, explanation for the presence of this tissue in the inguinal nodes and vulva. No other theory could possibly serve to explain the occurrence of endometrium in the brachioradialis muscle and thigh as reported by Navratil and Kramer, and by Mankin, respectively. In these 2 cases the fragments of endometrium would have to progress through the capillary bed in the lungs or pass from the right to the left heart through a patent foramen ovale.

In addition, pathologists occasionally find innocuous, normal syncytial cells in the lung tissue of women who have died during pregnancy or childbirth. It is also significant that in chorionepithelioma one of the first sites of

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metastasis is to the lungs. This is prima facie evidence that cells from the uterus can reach the lungs through the blood and lymphatic channels. Is there any reason why endometrial tissue cannot be transported in the same way? Might not aberrant endometrial tissue be the explanation for so called vicarious menstruation? Is it possible that ectopic endometrial tissue is the origin of heretofore unrecognized benign and malignant tumors of the lungs?

The desire to confirm our suspicion was crystallized by an interesting case observed by one of us (J. E. H.).

A woman 42 years of age complained of a small mass in one inguinal region which became larger and painful at the time of menstruation. In addition, she complained of hemoptysis, often associated with the menstrual period. The inguinal mass was diagnosed as an incarcerated omental hernia. The mass was explored and found to consist of large lymph nodes. These nodes were removed and microscopic examination showed them to contain endometrial tissue. Thereupon, it was suggested that the hemoptysis might be due to an endometrial implant in the lungs. This suggestion was considered whimsical by some of our colleagues. We conveyed our suggestion to our chief, Dr. Otto H. Schwarz, who thought our idea meritorious. He encouraged us to study the case further and to carry out some experimental work. Roentgenograms of the lungs showed a circumscribed shadow in the apex of the right lung. There was no clinical or definite x-ray evidence of tuberculosis. Repeated sputum examinations showed no tubercle bacilli. This small shadow then was considered by us possibly to be endometrial tissue. The patient refused to have a bronchoscopic examination and biopsy of the area. Some dilated veins were found in the pharynx, but never any evidence of bleeding. She was given a sterilizing dose of x-rays to the ovaries, in order to destroy hormone elaboration and thereby check the growth of the ectopic endometrium in the inguinal nodes. Since that time the patient has had cessation of menstruation and the groin has been free of tumors. Repeated x-ray plates of the chest have not revealed any appreciable change in the size of the aforementioned shadow. She occasionally has hemoptysis, usually associated with excitement. Repeated examinations have failed to show any evidence of tuberculosis.

Whether this case was one of endometrial transplant in the lung or not, is a matter of conjecture. Nevertheless, it stimulated our interest enough to attempt the transplantation of endometrial tissue into the lungs of a laboratory animal.

TECHNIQUE

In our original plan we decided to remove the uterus of the guinea pig, scrape away the endometrium, and transplant the tissue directly into the lung substance. We abandoned this plan without a single trial, for the obvious reason that the surgical shock of removal of the uterus and transplantation of the mucosa into the lung would almost surely kill the animal. Then we decided to remove the uterus, curette away the endometrium, grind it with a pestle and mortar, suspend the tissue in normal saline solution, and inject it into the lung tissue and pleural cavity. The uncertainty of placing the tissue in the desired location caused us to discard this plan of attack. Next we actually attempted to inject this suspended tissue into the inferior vena cava. The vein was difficult to isolate, very fragile and after removal of the needle, bleeding could not be controlled. In addition, considerable time was consumed in the abdominal cavity along with some traumatization, which helped to dispatch the animals. Out of this maelstrom of ideas, we evolved the technique followed in these experiments.

Large rabbits, weighing 2,200 grams, were used. Each of them was given 2,000 units of theelin intramuscularly 2 or 3 days prior to the operation in order to stimulate the endometrium to proliferate. The rabbits were given nembutal rectally in doses of 0.18 gram for analgesia and only small amounts of ether by inhalation were found necessary for the operation. A small portion of each horn, together with the uterus, was removed. While one operator ligated the pedicles and closed the abdominal wall, the other prepared the endometrial tissue curetted from the uterus. The tissue was ground up, suspended in normal saline, and injected into the ear vein. A No. 18 gauge needle was used and surprisingly large pieces of tissue could be forced through the lumen. This method has several advantages that are worth recounting. A large rabbit has a comparatively large uterus, which facilitates the technical part of the hysterectomy. It is obvious that more endometrial tissue is available. The pre-operative administration of theelin enhanced the growth of the endometrium and thereby facilitated

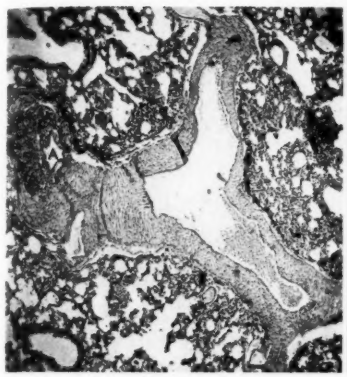

Fig. 1

Fig. 2

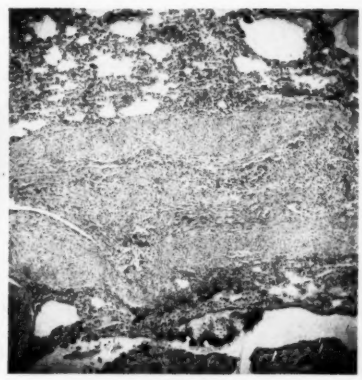

Fig. 3

Fig. 1. Rabbit 1981. *A* shows a small vein with typical endometrial stromal cells in the wall.

Fig. 2. Rabbit 1944. The left lung shows numerous grayish white patches which are not inflammatory in character. They are considered most likely to be endometrial stromal cells and fragmented endometrium, but not definite in character.

Fig. 3. Rabbit A-7. The thrombosed vessel shows fragments of epithelial tissue that are growing in the organized tissue.

denudation. The time consumed and trauma done in performing the hysterectomy was minimal, indeed. The injection of saline suspended endometrium into the ear vein is a very simple procedure and can be done with precision. The destination of the tissue is exactly the same as if it were injected into the inferior vena cava, namely, the right heart. From the right auricle it goes to the right ventricle and from there, through the pulmonary arteries to the lungs. A diffuse dissemination is insured.

A summary of the pathological findings follows:

PATHOLOGICAL EXAMINATION

Rabbit 1980. *Gross description.* Both lungs presented the same appearance. There were two or three hemorrhagic areas in the upper lobes. *Microscopic description.* No evidence of endometrial tissue. Some chronic passive congestion.

Rabbit 1981. *Gross description.* Both lungs showed several small grayish patches. *Microscopic description.* Left lung was normal. Right lung showed cells characteristic of stromal cells in the lumen of the veins (Fig. 1). No glandular epithelium was present.

Rabbit 1944. *Gross description.* The right lung had a mottled appearance. The middle lobe contained grayish-white spots which were quite well demarcated (Fig. 2). The left lung showed numerous grayish patches which were confluent. They stood out in relief against the normal lung tissue. *Microscopic description.* There were numerous small areas of necrosis. Some areas showed cells alien to the lungs which were not inflammatory cells. They may be endometrial stroma cells and fragmented epithelium but one cannot be certain.

Rabbit A-6. *Gross description.* Both lungs showed areas of grayish spots with a few reddish areas. *Microscopic description.* Both lungs appeared normal with the exception of some chronic passive congestion. No evidence of endometrial tissue.

Rabbit A-7. *Gross description.* The right lung had a grayish appearance. There were some irregular reddish-brown areas. There was a small amount of fibrinous exudate over the lower lobe. The left lung was covered by a fibrinous exudate. In the upper lobe there was a firm, irregular, white nodule, measuring 1.5 centimeters in diameter. On the posterior surface of the lower lobe was a small, round, bluish area. *Microscopic description.* The right lung showed marked extravasation of blood. There was no evidence of infection. The left lobe showed areas of necrosis. One thrombosed vessel showed fragmented glandular tissue (Fig. 3).

Rabbit A-8. *Gross description.* The posterior surface of the lower lobe of the right lung showed numerous grayish patches, many of which had a beaded appearance. The posterior surface of the left lung showed areas of bluish discoloration. There were two small hemorrhagic areas in the upper portion of the lower lobe. *Microscopic description.* Neither lung showed any evidence of endometrial tissue.

Rabbit A-9. *Gross description.* The right lung was covered by a white fibrinous exudate. The lower lobe showed a number of small, hard, white nodules. The left lung was also covered by a fibrinous exudate. The lower lobe showed a number of white

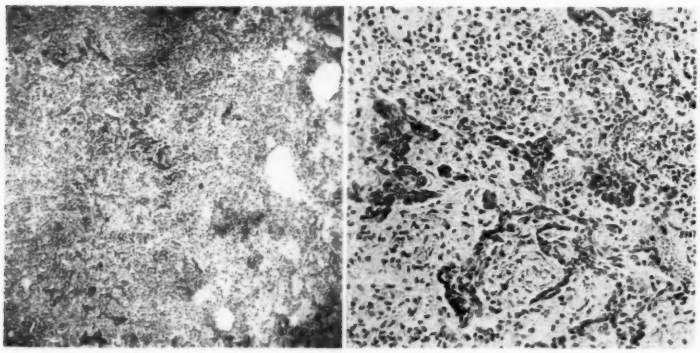

Fig. 4, left. Rabbit A-9. A diffuse distribution of endometrial stromal cells.
Fig. 5. Same rabbit. High power of section shown in Figure 4.

areas which had a tendency to be confluent. *Microscopic description.* The right lung showed numerous necrotic areas. One area showed fragmented epithelial tissue. One section through the left lung showed numerous strands of endometrial stromal cells about the capillaries (Figs. 4 and 5). Another section showed a large blood vessel lined with low cuboidal epithelium.

Rabbit A-10. *Gross description.* The right lung showed some fibrinous exudate over the surface and numerous grayish-white patches throughout. The left lung showed a fibrinous exudate over the surface. Both lobes showed localized patches of grayish and chocolate colored areas. *Microscopic description.* Both lungs showed numerous areas of necrosis.

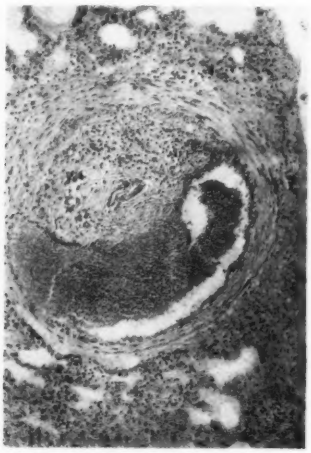

Fig. 6. Rabbit A-10. A large blood vessel which is partially occluded by an organized thrombus, which contains glandular tissue.

One section through the right lung showed a blood vessel in which there was an organized thrombus containing one endometrial gland intact and another one which was fragmented (Fig. 6).

Rabbit A-19. *Gross description.* Over the surface of the right lung there were several gray and some brownish-red spots. The anterior surface of the left lung showed some fibrinous exudate. In the lower lobe was a dark area measuring 1.5 centimeters in width. The posterior surface showed evidence of a fibrinous exudate. The lower two-thirds of the lower lobe was a chocolate color. Near the medial border was a cyst 1.5 centimeters in diameter. The cavity contained a small amount of thick chocolate-like material (Fig. 7). *Microscopic description.* One section through the right lung showed a blood vessel containing some débris and several cells resembling endometrial stroma. Sections through the left lung showed blood vessels which contained endometrial glands and stroma (Figs. 8, 9, 10, 11, and 12).

Rabbit A-23. *Gross description.* The upper lobe of the left lung was consolidated. There were numerous areas of grayish discoloration. The lower lobe showed a number of hemorrhagic areas. There were also numerous grayish nodules. The upper lobe of the right lung was occupied by white, hard nodules. There were hemorrhagic areas throughout the remainder of the lung. *Microscopic description.* The right lung showed no typical muellerian epithelium. The left lung showed several of the bronchi filled with nondescript débris. One region showed numerous small glands which were not bronchioles and are, therefore, considered to be endometrial in origin, although they are not characteristic (Figs. 13 and 14).

Only two or three blocks were taken from suspicious areas in each lung. Had we taken numerous or serial sections, perhaps the frequency would have been greater than we have recorded. We were interested to show that

Fig. 7

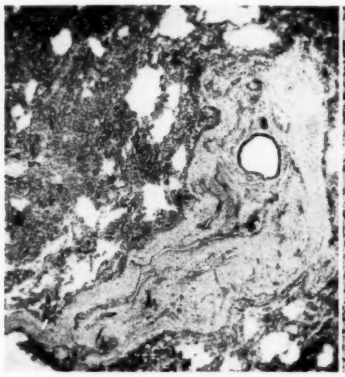

Fig. 8

Fig. 9

Fig. 7. Rabbit A-19. Note the cystic cavity which was filled with a chocolate-like material.

Fig. 8. Same rabbit. A thrombosed blood vessel which shows the presence of glandular tissue that is growing in it.

Fig. 9. Same rabbit. A high power magnification of Figure 8.

the tissue would grow in the lung and one case sufficed; therefore, we have made no effort to demonstrate extensive dissemination or frequency of implantation.

As controls we studied the lungs of 10 normal rabbits, used in the Friedman test for pregnancy. All of these showed normal lung tissue.

PURPOSE OF STUDY

The primary purpose of this investigation was to establish the fact that autotransplanted endometrial tissue would grow in the lungs. This we have demonstrated. These experiments have also revealed that endometrial tissue can be transported through the veins to the lungs. We have already pointed out

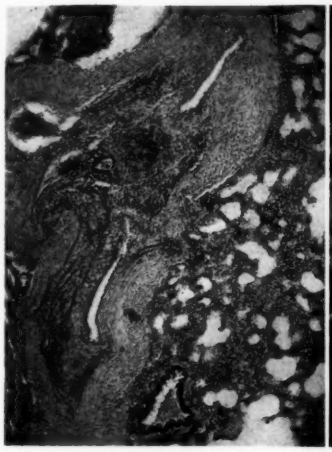

Fig. 10

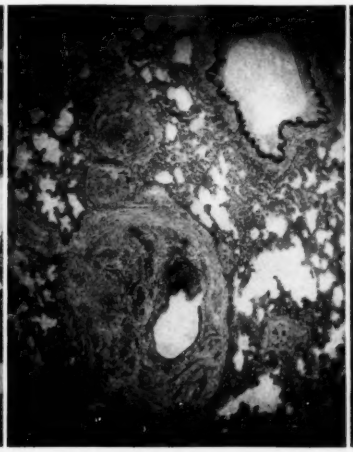

Fig. 11

Fig. 12

Fig. 10. Same rabbit. Another thrombosed vessel containing glands surrounded by endometrial stroma. The tissue has extended through the wall of the vessel.

Fig. 11. Same rabbit. Still another thrombosed vessel showing the presence of a diffuse growth of epithelium and stroma.

Fig. 12. Same rabbit. A high power of the large gland in Figure 11.

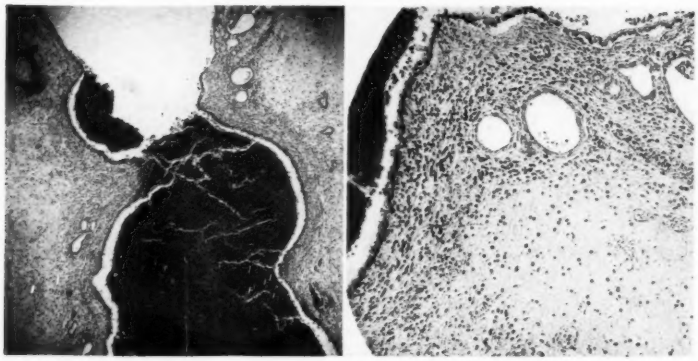

Fig. 13, left. Rabbit A-23. The large glandular structure is a bronchiole filled with inflammatory exudate. Outside of this one can see numerous small glands which are not typically endometrial but are alien to the lung.

Fig. 14. Same rabbit. A high power photomicrograph showing the character of the glands described in Figure 13.

that endometrial tissue has been demonstrated in the lumina of veins and lymphatics by other investigators, and an abundance of information has been recorded from which one can logically deduce that uterine mucosal tissue must be transported through the lymph and blood vascular systems. With the fact unequivocally established that endometrial tissue is transported through the lymphatic and blood vascular systems, and that the tissue will grow in the lungs, is it not logical to assume that uterine mucosa does occasionally become implanted in the lungs? Is it not also plausible that this tissue might rarely be found in any organ in the body, since it may get into the left heart either by passing through a patent foramen ovale or by propagating through the capillaries of the lungs into the pulmonary veins and thence into the left heart?

With this possibility of wide dissemination in mind, a credible theory for the explanation of vicarious menstruation becomes evident. Vicarious menstruation may be due to endometrial transplants in the area from which the periodic bloody discharge issues. In vicarious menstruation the bleeding usually takes place from the nose or some open sore, though it may come from almost any mucous surface such as the lungs, bladder, rectum, and stomach. The axilla and groin may be affected. Vicarious menstruation is very rare, and physicians who are fortunate enough to see accessible areas which have a discharge of blood associated with the menstrual period should make a detailed microscopic study and record the findings.

Another interesting phase of this subject, which needs further investigation, is the development of malignancy in ectopic tissue. Aberrant endometrium shares with normal endometrium the capacity for becoming malignant. The fact that this tissue has a lymphogenous and hematogenous distribution, its ability to invade by direct continuity not only the parent organ but any alien host and its proliferative activity in an ectopic existence, are characteristics which are common to malignant tissue. We, therefore, suspect that this heterotopic tissue has a running start toward malignant development. Many primary glandular carcinomas of the ovaries whose origin was formerly nebulous, are now conceded to arise from endometrial implants. This may apply in other locations. Uterine mucosa may change its morphological aspects considerably in adapting itself to an ectopic environment. One must be cognizant of this protean characteristic in order to recognize the tissue in its various aberrant locations. This distortion is particularly noticeable in cancerous change.

The mortality in our experiments was very great. However, all of the rabbits lived 19

days and over. The explanation for this high mortality is obviously due to the enormous amount of tissue injected into the veins. It was surprising that the animals were not dispatched immediately. The tissue spontaneously disseminated through the veins would be infinitesimal as compared to the large amounts injected in these experiments.

We shall report at a future date on some additional work we have started. We have done hysterotomies on several animals and have removed the mucosa and sutured the horns. The mucosal tissue has been injected into the ear vein. The animals will be bred. We hope to show a decidual reaction in the implants in the lungs.

CONCLUSIONS

A study of these experiments, clinical and pathological observation, and information gleaned from the literature, make the following conclusions seem evident.

1. Endometrial tissue is transported through lymphatics and veins.

2. Autotransplanted uterine mucosa of the rabbit will grow in the lung tissue.

3. With these two conclusions as a major premise, we can conclude that, therefore, endometrial tissue must occasionally reach the lungs and grow.

4. A plausible explanation for vicarious menstruation is evident, since endometrial tissue can get into the general circulation either through a patent foramen ovale or by propagation through the pulmonary circulation.

5. This aberrant endometrial tissue has characteristics which would indicate it has increased potentiality to become malignant.

Dr. Howard A. McCordock, late professor of pathology in the Washington University School of Medicine, gave valuable assistance in the microscopic study of these lung preparations.

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THE EFFECT OF OBSTETRICAL ANESTHESIA UPON THE OXYGENATION OF MATERNAL AND FETAL BLOOD WITH PARTICULAR REFERENCE TO CYCLOPROPANE

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IN recent years asphyxia and atelectasis at birth have assumed primary importance among the causes of neonatal death. As the mortality from intracranial hemorrhage yields to obstetrical knowledge and skill, problems associated with respiration demand and are receiving increased attention. That this attention be based upon fundamental physiological facts is essential. Clinical observation and speculation are insufficient. Thus, after many years of observation, theory, and controversy in the literature, actual biochemical measurements such as those reported by Eastman (4) and his colleagues have offered for the first time a factual basis upon which an understanding of the onset of human respiration can be built.

These authors first described a simple technique for obtaining samples of umbilical cord blood representative of the arterial and venous sides of the infant's circulation at, and even before, delivery. Using this method they demonstrated that the fetus exists in utero at a low level of blood oxygenation, and that this apparently physiological anoxemia may be considerably increased during labor, so that at delivery the infant's blood is usually surprisingly deficient in oxygen. Moreover, they demonstrated that because of accumulation of lactic acid from the maternal organism, the newborn infant's blood is not only anoxemic but also tends toward an acidosis and toward an increased carbon dioxide tension. These three factors, namely, anoxemia, acidosis, and increased carbon dioxide tension, Eastman showed to be present in still greater degree in infants presenting the clinical picture of asphyxia neonatorum.

That a disturbance of the respiratory physiology in mother and infant may result directly from maternal anesthesia at delivery was demonstrated in a fifth paper by Eastman (6) published in 1936. In this study, data were presented upon the cord bloods of infants born under chloroform, ether, and nitrous oxide-oxygen anesthesias. While in mothers receiving chloroform and ether the usual oxygenation of the fetal blood was unaffected, nitrous oxide-oxygen mixtures were regularly associated with some degree of abnormal anoxemia, moderate in the mother and relatively marked in the fetus. This state was augmented when stronger concentrations of nitrous oxide were administered to deepen the maternal anesthesia. When infants born to such mothers showed clinical asphyxia, their cord bloods presented levels of oxygen as low as 1.5 to 10.4 per cent of capacity.

It has been found the arterial blood of the normal adult is saturated to about 95 per cent of oxygen capacity, that of the fetus at birth about 50 per cent saturation. The author stressed the conclusion that asphyxia neonatorum is an example of profound oxygen want. "For this reason," he declared, "the one urgent necessity in its treatment is oxygen, and by the same token, the one urgent requirement in its prevention is oxygen."

In a more recent study of asphyxia, Wilson, Torrey and Johnson state that the most accurate index of the gravity of a particular case of asphyxia neonatorum is supplied by a blood analysis. These authors report oxygen contents of from 0.8 to 3.6 volumes per cent in the cord bloods of 9 infants selected as cases of asphyxia pallida. Expressed as percentage saturation of hemoglobin, to conform with the figures in the foregoing paragraph, these values would approximate 3.5 to 17.0 per cent saturation. Again, deficiency in oxygenation of fetal blood is stressed as a constant finding in severe asphyxia.

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Such reports arouse the curiosity of anyone observing a large number of newborn infants. It was felt that a series of observations upon routine deliveries at the Boston Lying-in Hospital would give desirable information as to the effects of the various anesthetics usually employed there, and that something might be learned also by studying the effect of a new anesthetic agent, namely, cyclopropane. Whatever results were obtained, whether exactly similar to those of other investigators or not, would establish normal controls for further studies in this clinic. Since other investigators had placed so much stress upon the condition of the blood as regards oxygen, it was decided at first to confine data to that single biochemical factor. Undoubtedly the hydrogen ion and carbon dioxide relationships are also of importance to an understanding of maternal and fetal respiration.

METHODS

In Eastman's studies specimens of maternal blood were obtained from an arm vein at delivery. The work of Haselhorst and Stromberger indicates that the oxygenation of venous blood in the arm is reasonably representative of the state of blood in the uterine veins. However, of much greater interest than the oxygenation of blood returning to the mother's heart is the state of her arterial blood as it arrives at the uterus. We considered it of interest to determine the arterial as well as the venous oxygen content in a representative number of mothers under each type of anesthetic studied. Since arterial blood from an extremity should not differ from that in the uterine arteries, the radial artery was used for puncture. Accordingly, an attempt was made to obtain 4 blood specimens at or immediately following the infant's delivery. These were: (1 and 2) fetal arterial and venous blood from the umbilical vein and umbilical arteries, respectively; (3), maternal arterial blood from the radial artery; and (4), maternal venous blood from a vein of the same arm.

Exact synchronization of sampling was not always possible, usually because of difficulty in arterial puncture. It may be stated, however, that the umbilical cord bloods were in all cases representative of fetal conditions before or at the moment of the infant's first breath, and that the most delayed maternal specimens were taken within a maximum of 2 minutes thereafter.

In our early work blood was taken into an oiled syringe and preserved under oil with heparin as an anti-coagulant. Because of the marked solubility of cyclopropane in oil, this method was later abandoned for the ingenious procedure of Adriani, in which blood is collected and stored with oxalate over mercury in a glass syringe. Oxygen content and capacity were determined by the method of Van Slyke and Neill; in the presence of ether the technique was modified according to that of Shaw and Downing (12). In samples containing nitrous oxide or cyclopropane, the method of Orcutt and Waters was used. Except in rare instances when specimens were insufficient, determinations were made in duplicate. In many instances determinations of carbon dioxide and hydrogen-ion concentration were done upon the same bloods.

The anesthesias were administered by the staff anesthetists of the hospital. The usual routine procedures were used, except that in nitrous oxide-oxygen administration, the anesthetist sometimes had to deepen the anesthesia beyond the stage customary in this clinic so that relaxation sufficient for arterial puncture could be obtained. The amount of nitrous oxide in the mixture was never knowingly more than 80 per cent even on such occasions. Deeper relaxation is ordinarily secured in this clinic by the addition of ether vapor to the nitrous oxide-oxygen mixture. Such anesthesia was not used in these studies because it was found impossible to analyze blood accurately for oxygen in the presence of both ether and nitrous oxide. Where ether was given alone, the ordinary open drop method was used in almost all instances. One case of ether vapor is included.

Cyclopropane was administered according to the method of Waters and Schmidt. In this technique, which is more or less standard, the system is a closed one so that the only gases involved are the nitrogen in the patient's lungs at the outset, carbon dioxide which is removed by soda-lime unless maternal apnea threatens, cyclopropane, and oyxgen. The

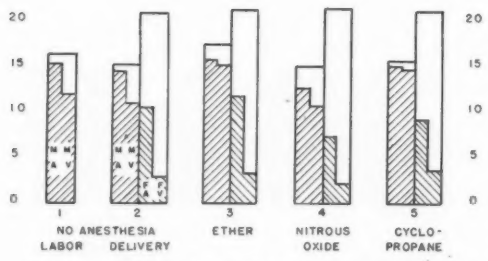

Chart 1.—Maternal and fetal oxygen relationships. M. A.—maternal arterial; M. V.—maternal venous; F. A.—fetal arterial; F. V.—fetal venous. The height of the column represents volumes per cent of oxygen capacity (plain), and of oxygen content (shaded). Second diagram from data published by Eastman (4).

mixture breathed by the patient at the time of actual delivery is calculated to contain about 15 per cent cyclopropane, about 80 per cent oxygen, and the rest small amounts of nitrogen and carbon dioxide. The usual period of anesthesia before delivery was from 5 to 15 minutes. In maternal specimens drawn during cyclopropane administration it was often impossible to tell the venous from the arterial specimen by a difference in color.

Practically all patients received some preliminary medication, usually sodium amytal 3 to 6 grains and scopolamine, 1/150 grain. This is in a way unfortunate as it introduces a variable factor in our results. However, we have not been able to determine a specific effect of the type or amount of medication used upon the degree of oxygenation of fetal blood, nor, except in a very general way, upon the promptness of respiratory onset. Moreover, since it was desired to determine the biochemical status of the average baby born in this clinic, the customary medication was not omitted in the mothers and infants studied.

RESULTS

In order to measure the specific effect of anesthesia upon the maternal blood, determinations were first made upon the arterial and venous blood of 10 women during labor, but before the administration of anesthesia for delivery. The results of these determinations are given in Table I, and comprise the first columns in Chart 1. It will be seen that the level of oxygenation of arterial blood is

TABLE I.—BLOOD OF PATIENTS DURING LABOR, BUT BEFORE DELIVERY

Patient	Oxygen capacity	Arterial oxygen		Venous oxygen	
		Content	Per cent	Content	Per cent
No. 1	16.8	14.9	88.5	10.8	64.2
No. 2	17.2	16.0	93.3	12.9	75.0
No. 3	12.4	11.1	89.2	5.6	45.1
No. 4	18.2	15.5	85.6	10.9	60.0
No. 5	19.0	18.3	96.0	16.9	88.6
No. 6	15.3	13.8	90.5	12.6	82.4
No. 7	17.7	16.6	93.8	11.2	63.3
No. 8	16.4	14.4	88.0	11.8	72.0
No. 9	17.5	16.1	92.0	12.4	70.8
No. 10	17.6	17.0	96.6	15.8	89.8
Average	16.8	15.4	91.3	12.1	71.1

slightly below the usually accepted figure of 95 per cent saturation, probably because of the actual physical work involved in labor. These figures and those to follow may be compared with data from a series of 15 normal deliveries without anesthesia in which Eastman (4) obtained the averages for maternal and fetal blood shown in the following table.

EASTMAN'S STATISTICS

	Maternal	Fetal
Oxygen capacity—volumes per cent	15.4	20.8
Arterial oxygen content—volumes per cent	14.7*	10.5
Saturation—per cent	95.0*	50.5
Venous oxygen content—volumes per cent	11.0	3.3
Saturation—per cent	71.3	15.8

*Estimated.

For purposes of graphic comparison, these figures have been used as the basis for the second diagram in Chart 1. It will be noted that in our series of maternal bloods before anesthesia and delivery, the figure for venous blood is much the same as that for unanesthetized women at the moment of delivery.

For 21 deliveries under ether anesthesia, our data are given in Table II and in the third diagram of Chart 1. The type of delivery was usually normal, as is indicated in the table. With ether as with the other anesthetics studied some operative deliveries are included.

The following phenomena would appear to be associated with ether anesthesia: (1) A rise in oxygen capacity of the maternal blood; (2) a diminution in percentage saturation of maternal arterial blood. This, because of the

TABLE II.—DELIVERIES UNDER ETHER

Delivery*	Maternal					Onset of respiration**	Fetal				
	Oxygen capacity	Arterial oxygen	Per cent	Venous oxygen	Per cent		Oxygen capacity	Arterial oxygen	Per cent	Venous oxygen	Per cent
1 N.D.	17.6	15.7	89.2	14.3	81.2	B	23.6	13.0	55.0	3.1	13.0
2 L.F.	18.4	15.7	85.3	16.4	89.6	C	21.3	9.4	44.2	3.7	17.4
3 N.D.	15.3	14.4	94.0	13.1	85.6	A	21.4	12.0	56.1	5.1	23.8
4 N.D.	17.7	16.9	95.4	15.7	88.6	B	21.6	14.1	65.3	5.0	23.2
5 N.D.	18.3	18.2	99.0	17.3	94.5	A	21.0	9.2	44.0	1.4	6.7
Average of 5	17.5	16.2	92.6	15.3	87.9		21.8	11.5	53.0	3.6	16.8
6 N.D.	15.9			13.6	84.9	A	21.3	10.2	50.2	0.4	1.7
7 N.D.	19.7			15.9	80.8	A	19.2	15.7	81.7	2.1	10.9
8 L.F.	18.0			16.2	89.9	A	20.2	14.7	72.8	6.1	30.2
9 L.F.	18.2			14.4	79.1	C	21.5	13.9	64.7	6.7	31.1
10 N.D.	17.4			15.2	87.4	B	21.9	12.9	59.9	3.5	16.0
11 N.D.	17.9			15.9	88.8	A	21.3	12.1	56.8	0.8	3.8
Average of 11	17.6			15.3	86.4		21.3	12.5	59.2	3.3	16.2
12 N.D.						A	21.4	3.5	16.3	1.0	4.7
13 Breech						C	20.1	11.4	56.7	1.5	7.5
14 L.F.						A	20.4	9.5	46.6	1.8	8.8
15 L.F.						A	23.1	13.5	58.4	5.4	23.4
16 N.D.						C	20.8	16.1	77.4	6.2	29.8
17 L.F.						A	19.9	15.7	78.9	8.8	44.2
18 N.D.						A	21.9	9.7	44.2	1.8	8.2
19 N.D.						A	20.5	12.0	58.5	2.4	11.7
20 Breech						A	22.4	11.2	50.1	1.4	6.2
21 N.D.						A	22.4	13.6	60.7	2.1	9.4
Average of 21							21.3	12.0	57.1	3.3	15.8

*N. D.—Normal delivery; L. F.—low forceps.
**A—Immediate; B—delayed; C—delayed and resuscitation required.

increase in oxygen capacity just mentioned, is not necessarily accompanied by an actual decrease in volumes per cent of oxygen carried in the arterial blood. (3) A considerable increase in the oxygen saturation of the maternal venous blood, with a lessened arteriovenous difference. The average figures from the 21 infants show very little deviation from Eastman's figures for infants born without anesthesia.

Data from 20 deliveries, which included 21 infants, under nitrous oxide-oxygen anesthesia are given in Table III and Chart 1. A definite oxygen deficit in the maternal arterial blood was noted in all the 5 specimens. Oxygenation of maternal venous blood was practically the same as that in venous blood from unanesthetized mothers, but the fetal blood showed more anoxemia than with either of the other anesthesias studied.

For cyclopropane anesthesia the figures from 19 deliveries in Table IV show the very high oxygenation not only of the arterial but also of the venous blood in the mother. In several individual instances identical values for the arterial and venous sides were obtained. Such results must be due to technical inaccuracies within the limits of error of the method, but obviously they indicate a very narrow arteriovenous difference. Notwithstanding the excessive saturation of venous blood with oxygen—in fact, perhaps because of it, as will be discussed later—the fetal bloods occasionally were very poorly oxygen-

TABLE III.—DELIVERIES UNDER NITROUS OXIDE-OXYGEN

Delivery**	Maternal					Onset of respiration**	Fetal				
	Oxygen capacity	Arterial oxygen	Per cent	Venous oxygen	Per cent		Oxygen capacity	Arterial oxygen	Per cent	Venous oxygen	Per cent
1 N.D.	13.5	12.5	92.6	10.2	75.5	B	22.7	5.5	24.2	1.2	5.3
2 N.D.	15.3	13.5	88.1	10.6	69.3	A	21.7	9.9	45.6	1.8	8.3
3 N.D.	15.0	12.8	85.3	11.7	77.9	A	22.7	12.4	54.6	3.7	16.3
4 L.F.	13.3	12.1	91.0	9.4	70.7	A A Twin	– (18.3 – (19.1	6.4 3.2	35.0 16.8	3.0 0.9	16.4 4.7
5 N.D.	17.9	13.2	73.7	10.9	60.9	A	20.1	8.9	44.3	1.4	7.0
Average of 5	15.0	12.8	86.2	10.6	70.9	Average of 6	20.8	7.7	33.4	2.0	9.7
6 N.D.	14.5			10.5	72.4	A	20.7	8.5	41.1	5.4	25.8
7 N.D.	17.6			13.4	76.1	A	20.8	8.9	42.8		
8 N.D.	17.7			12.8	72.3	B	21.2	2.5	11.8	0.5	2.4
9 N.D.	17.6			15.3	86.9	A	19.6	8.9	45.4	0.8	4.1
10 N.D.	14.3			10.4	72.7	A	21.3	8.0	37.6	2.8	13.1
Average of 10	15.7			11.5	73.5	Average of 11	20.7	7.5	36.3	2.2*	10.3*
11 N.D.						A	26.5	15.8	59.6	3.7	14.0
12 N.D.						A	20.9	8.5	40.6	1.3	6.5
13 N.D.						A	20.4	7.1	4.8	2.5	12.3
14 N.D.						A	22.7	1.9	8.3	0.5	2.2
15 L.F.						A	21.5	8.0	37.2		
16 N.D.						A	21.2	2.3	10.8	1.5	7.1
17 N.D.						A	24.6	3.0	12.2	0.7	2.8
18 N.D.						A	22.9	1.4	6.1		
19 N D.						A	22.0	11.0	52.7		
20 N.D.						A	21.2	4.9	23.1	4.4	20.8
Average of 21							21.5	7.0	32.6	2.1‡	9.0‡

*Average of 10.
‡Average of 17.
**See Table II for explanation of symbols.

ated and on an average showed values below those obtained with ether anesthesia.

Before entering upon a general discussion of these results, some comment is necessary regarding the wide variations in the data for any one of the three anesthetics. This is most obvious in the figures for fetal bloods in the tables representing deliveries under nitrous oxide and cyclopropane. For example, in Table III, patients 1 and 3 are both representative of normal deliveries under nitrous oxide-oxygen, yet one infant is delivered with more than twice as much oxygenation of arterial blood as the other. In fact, it will be noted in the twin infants born to patient 4 in the same table that, although born from the same uterus about 4 minutes apart, the blood of the second twin is only about half as well oxygenated as that of the first.

Anatomical and other fortuitous circumstances must play a large part in producing such variations. The element of time is probably of importance, as shown by the lower value in the blood of the second twin. Barcroft has even observed simultaneous specimens from 2 cotyledons of the same placenta in sheep to differ by as much as 50 per cent in oxygen saturation. Such facts would indicate that some scattering of results might be expected in a study such as this one, but the differences between averages for the anesthetics are so great as to indicate a specific effect upon both the mother and the child for each of them.

TABLE IV.—DELIVERIES UNDER CYCLOPROPANE

Delivery**	Maternal					Onset of respiration**	Fetal				
	Oxygen capacity	Arterial oxygen	Per cent	Venous oxygen	Per cent		Oxygen capacity	Arterial oxygen	Per cent	Venous oxygen	Per cent
1 N.D.	15.9	15.9	100.0	14.8	93.0	A	19.6	11.3	57.6	5.9	30.1
2 N.D.	16.1	16.1	100.0	16.1	100.0	A	22.6	8.1	35.8	2.2	9.7
3 N.D.	13.1	10.9	83.3	10.9	83.3	A	21.9	6.8	31.0	0.7	3.2
4 N.D.	17.0	17.0	100.0	17.0	100.0	C	19.8	0.7	3.5	0.6	3.0
5 N.D.	10.6	10.6	100.0	10.4	98.1	B	18.6	8.3	44.6	4.4	23.6
6 N.D.	15.7	15.5	98.7	15.6	99.4	B	20.9	14.7	70.4	3.7	17.7
7 N.D.	14.5	14.5	100.0	14.4	99.3	B	21.7	10.5	48.4	1.4	6.4
8 N.D.	16.7	16.7	100.0	16.2	97.0	A	22.1	1.9	8.6	0.9	4.0
9 N.D.	17.6	17.5	99.5	17.2	98.0	C	20.5	13.0	63.4	5.7	27.8
10 N.D.	17.8	15.2	85.5	15.1	85.0	B	19.5	13.4	68.6	9.1	46.6
11 N.D.	17.9	16.8	94.0	15.6	87.6	A	20.5	7.8	38.1		
12 N.D.	14.3	13.5	94.4	13.0	91.0	A	22.6	12.5	69.1		
Average of 12	15.6	15.0	96.5	14.7	94.5		20.8	9.1	44.9	3.5*	17.2*
13 Caes.	18.5			15.3	82.6	A	23.3	8.2	35.2	2.8	11.5
14 L.F.	17.3			14.2	82.0	A	22.2	10.4	46.8	4.3	19.4
15 L.F.	15.3			15.0	98.0	A	20.9	13.8	66.1		
16 Caes.	17.8			16.9	94.9	A	22.4	3.3	14.7	1.6	7.1
Average of 16	16.0			14.7	92.9		21.2	9.0	43.8	3.3‡	16.2‡
17 L.F.						C	19.8	13.0	65.6	9.5	48.0
18 L.F.						A	22.9	15.4	67.3	3.4	14.5
19 Caes.						A	20.8	1.1	5.0	0.9	4.0
Average of 19							21.2	9.2	44.0	3.6†	17.0†

*Average of 10.
‡Average of 13.
†Average of 16.
**See Table II for explanation of symbols.

MATERNAL ANESTHESIA AND FETAL ANOXEMIA

Chart 1 indicates graphically that the three anesthetic agents produced, in a general way, three quite different chemical pictures in the patients studied. The use of ether appears to offer the least disturbance of normal oxygenation of fetal blood. In maternal blood it produces definite alterations not only in oxygen content but also in oxygen capacity. The result of these alterations would be to carry a normal or even more than normal supply of oxygen to the maternal side of the placenta. The arteriovenous difference is diminished in the mother, but a sufficient supply of oxygen reaches the infant in spite of the large amount returning to the heart in the mother's veins.

Changes exactly similar to those just described in the maternal blood have been demonstrated experimentally in dogs by Shaw, Steele, and Lamb (13). These workers found, however, that with prolonged administration of ether, the arterial oxygen content fell off progressively, so that in time a state of anoxemia might result. However, for routine deliveries, ether, properly administered, appears to insure satisfactory oxygenation of maternal and fetal blood. It was hoped that in individual infants born with exceptionally good oxygenation, some particular and informative conditions would appear in the maternal blood, but examination of the table does not reveal any special maternal condition which constantly accompanies the higher fetal values.

Table III and Chart 1 show very definite results from nitrous oxide-oxygen administra-

tion. The effect of this agent was to reduce the amount of oxygen in maternal arterial blood to an average of only 12.8 volumes per cent of oxygen, as against the comparable figure of 16.2 volumes per cent for ether. The fetal blood suffers proportionately. Apparently the head of pressure under which oxygen arrives at the uterus under these circumstances is simply not sufficient to produce diffusion of a proper amount of oxygen through the placenta to the fetus. This fact has been emphasized by Eastman (6). That such surprisingly low levels as 1.4 and 1.9 volumes per cent of oxygen in fetal blood could be reached in occasional normal deliveries with a supposedly safe mixture of nitrous oxide and oxygen makes this confirmation of his studies worth reporting.

With cyclopropane very interesting relationships of maternal and fetal blood occur. It has frequently been noted by surgeons operating upon patients with this anesthetic that the color of the patient remains pink at all times and that the color of the venous blood is seldom as dark as with other anesthetics. Eversole and Overholt report that in thoracic operations upon patients with lowered vital capacities, the venous and arterial bloods are indistinguishable. The same fact was noted in the present study. This redness of the blood on both sides of the circulation, which may be described as a decrease in the arteriovenous difference or as an arterialization of the venous blood, is usually ascribed to the large amount of oxygen administered with cyclopropane.

Actually, the belief that in the normal individual, i. e., in the absence of pneumonia or cardiac disease, the breathing of high oxygen concentrations will increase the saturation of the venous blood appreciably, is not physiologically sound. Normally, respiration of ordinary air produces saturation of arterial blood to 95 per cent capacity; the slight further increase possible with oxygen administration can alter the venous content only very slightly. Barach and Woodwell report determinations of oxygen content after normal subjects had breathed pure oxygen for 30 minutes. After 3 such experiments, the venous blood was found to be from 69 to 83 per cent saturated with oxygen. A normal subject in our laboratory breathed pure oxygen from a mask for 2 periods of 20 minutes each. After 1 period his venous blood was only 70 per cent saturated, after the other it reached 73 per cent. Thus the much greater oxygen saturation of venous blood observed under administration of 80 per cent oxygen and 20 per cent cyclopropane (Table IV) must be due to a specific effect of the cyclopropane itself, and not to the increased oxygen concentration in the mixture.

The specific manner in which cyclopropane produces this arterialization of venous blood must be by means of increased velocity of blood flow; probably associated with dilatation of arterioles and capillaries. This phenomenon has been shown to take place under ether, with the resulting decrease in arteriovenous difference shown in the diagram for that anesthesia in Chart 1. Our findings on the bloods of 12 mothers delivered under cyclopropane show a still smaller arteriovenous difference for this agent than for ether. It is suggested that workers in the field of capillary microscopy might verify this effect by direct observation of vasomotor conditions in patients anesthetized with this agent.

If the blood of the mother is being returned to the right heart with practically the same oxygen tension as it had in the aorta, there may be a diminution in the amount of oxygen taken up by the tissues. It is of interest to note that the average oxygenation of fetal blood under maternal cyclopropane anesthesia was considerably below that under ether. It is perhaps unjustifiable to view the state of fetal hemoglobin as reflecting the condition of the maternal tissues, but the extremely low oxygenation of the fetal blood in certain cases where simultaneous maternal arterial and venous specimens have been 100 per cent saturated make this an interesting hypothesis. In any event, the figures would indicate that a certain false sense of security, as to the condition of the infant, might arise from considerations based solely upon the appearance of the maternal blood.

Judged, then, from the standpoint of proper oxygenation of fetal blood during delivery, these observations indicate cyclopropane anes-

thesia, as administered in this clinic, to be more advantageous than nitrous oxide-oxygen, but considerably less satisfactory than ether.

FETAL ANOXEMIA AND ASPHYXIA NEONATORUM

At the inception of this study a definite correlation was anticipated between promptness of respiration and degree of anoxemia in individual infants. The two series of severely asphyxiated infants reported by Eastman (5) and by Wilson, Torrey and Johnson, had regularly shown an extremely low oxygenation of blood at delivery. From their figures it was inferred that asphyxia was almost to be expected in any infant whose arterial blood carried less than about 3 volumes per cent of oxygen.

In order to correlate fetal anoxemia and asphyxia neonatorum, the 61 infants whose blood was studied were arbitrarily graded as to the onset of respiration. The symbol "A" was used for infants breathing and crying lustily and immediately. There were 45 such infants. Very light and feeble respiration, or a delay in onset not sufficient to warrant attempts at resuscitation, was designated as "B." There were 9 infants in this group. The 7 infants remaining required some degree of resuscitation of a simple type and not prolonged beyond a few minutes by the obstetrician. This group was designated as "C." This impressionistic classification was found to be more informative than actual measurements of time elapsed before the first breath. However, it soon became apparent that these varying degrees of apnea were not constantly accompanied by the expected alterations in oxygenation of the infant's blood. While no babies in the series were critically asphyxiated, the variations in the onset of respiration were significant enough to be graded easily, yet this grading was not borne out by significant differences in the laboratory findings. This will be seen in Tables II, III, and IV, and more especially in Table V, in which the data from fetal bloods are grouped according to presence or absence of apnea at birth. Only in the 2 "slow" babies delivered under nitrous oxide-oxygen is there a definite correlation between anoxemia and apnea.

Whatever explanation may be offered for this lack of correlation must explain 2 types of results: first, those infants who were active and breathed at once, or Class A, but whose cord blood was definitely anoxemic; and second, those infants with some degree of apnea, or Classes B and C, whose blood showed average or better than average saturation with oxygen. Two explanations are possible. The first is that marked anoxemia at delivery bears no etiological relationship to asphyxia neonatorum. The studies of Eastman, and of Wilson and his colleagues, on definitely asphyxiated babies are too convincing to make this tenable. The second explanation is that anoxemia represents but one of several factors which, carried to a certain extent, and perhaps acting in summation, may interfere with the normal onset of respiration. On the basis of the results reported in the present communication, this latter explanation would seem to be the correct one. An interesting corollary of this hypothesis is the very apparent fact that the fetus can occasionally stand remarkably low levels of oxygenation, although probably for very brief periods, and still be capable of normal respiration. One wonders if, were it possible to analyze blood from the apneic baby a few minutes after the cord is clamped but before breathing begins, still greater degrees of anoxemia might not be demonstrated.

The other factors which also act to produce apnea in infants with satisfactory oxygenation of blood at birth, would of course include the variable elements of time and of direct physical trauma in delivery, the pre-anesthetic medication, the direct narcotic effect of obstetrical anesthesia upon the central nervous system of the fetus, and probably such other biochemical factors as the hydrogen ion content of the fetal blood and its carbon dioxide tension. The first of these we do not attempt to discuss beyond listing the type of each delivery in the tables. A tabulation of the amount of pre-anesthetic medication used in the deliveries studied is too cumbersome to be presented, but showed that mothers of the babies graded B and C received on the average slightly more medication than did the mothers of those babies breathing actively and at once.

TABLE V.—RELATION OF APNEA TO OXYGENATION OF FETAL BLOOD

Onset of respiration	Volumes per cent oxygen in blood: Arterial	Venous
Ether		
14 A*	11.6	2.9
3 B**	13.3	3.9
4 C†	12.4	4.5
Nitrous oxide		
19 A	7.3	2.3
2 B	4.0	0.85
Cyclopropane		
12 A	8.4	2.5
4 B	11.7	4.6
3 C	8.9	5.3

*A—Immediate.
**B—Slightly delayed.
†C—Delayed.

TABLE VI.—VOLUMES PER CENT OF ANESTHETIC IN MATERNAL AND FETAL BLOODS

Anesthetic	Maternal: Arterial	Maternal: Venous	Fetal: Arterial	Fetal: Venous
Nitrous oxide—average	28.0	21.7	13.5	9.8
Cyclopropane—average	7.5	6.7	6.0	5.1

As to the direct effect of the anesthetic administered to the mother, and reaching the infant's central nervous system by way of the placenta and fetal circulation a small amount of suggestive data can be offered from this study. While it was not possible to determine the relative amounts of ether in maternal and fetal blood at birth, the method of Orcutt and Waters offers an apparently accurate measurement of the volumes per cent of nitrous oxide or of cyclopropane present in any specimen of blood to be analyzed. Table VI shows how much of the anesthetic gas was actually present in the maternal and fetal blood at the time the cord was clamped in deliveries under those anesthetics. It is notable that with nitrous oxide-oxygen, in which the number of apneic infants was very small, the infant at birth had less than half as much anesthetic in his blood as was present in the maternal blood. In cyclopropane deliveries, in which there were more apneic infants, the concentration of the anesthetic was almost as high in the fetal as in the maternal circulation. Just how important the narcosis produced by anesthesia of the infant is, as a cause of critical asphyxia, remains to be determined. These results would indicate that it exerts a specific effect which cannot be neglected. Finally, it is to be hoped that the place of disturbed acid-base relationship and of carbon dioxide tension may be evaluated by further study.

SUMMARY AND CONCLUSIONS

Determinations were made of the oxygen content of arterial and venous blood from women during labor. Similar determinations were made upon the arterial and venous bloods of 3 groups of mothers and their infants at the moment of birth. These 3 groups represented routine deliveries under ether, under nitrous oxide-oxygen, and under cyclopropane anesthesia. In the second and third of these groups, the amounts of nitrous oxide and of cyclopropane were also quantitatively determined in the maternal and fetal bloods. An attempt was made to correlate the degree of oxygenation of maternal and fetal blood with the type of anesthetic used, and to discover the relationship between fetal anoxemia and the presence or absence of apnea in the newborn infant. The following observations seem significant:

1. Oxygenation of maternal blood during labor but before delivery and anesthesia was comparable to that observed by other authors for maternal blood at delivery without anesthesia. The arterial blood during labor showed a slight anoxemia.

2. Specimens of fetal blood at the moment of birth showed wide variations in oxygen content, presumably because of anatomical and other uncontrollable circumstances. As a rule, the fetal blood at birth, even on the arterial side, was considerably deficient in oxygen.

3. In general, ether anesthesia produced a definite elevation of the maternal oxygen capacity, and of the oxygenation of maternal venous blood. Under this anesthesia the fetal oxygenation appeared to be satisfactory.

4. Nitrous oxide, administered with at least 20 per cent oxygen, produced a definite maternal and fetal anoxemia.

5. Under cyclopropane, the maternal blood showed a pronounced elevation of oxygenation in both the arterial and venous specimens.

The cause of this phenomenon is discussed. It is probably not due to the high concentration of oxygen administered with cyclopropane. The blood of infants delivered under this agent was somewhat better oxygenated than those born under oxide-oxygen. It contained less oxygen than the blood of infants delivered under ether, or that reported in the literature for those delivered without maternal anesthesia.

6. Pronounced anoxemia in the fetal blood at birth was not constantly accompanied by apnea of the newly born infant, except in babies delivered under nitrous oxide-oxygen. Fetal anoxemia is probably one of several factors which may operate to produce apnea. A surprising degree of fetal anoxemia may be associated with a normal onset of respiration.

7. Cyclopropane was present in the fetal blood in almost as high concentration as in the maternal blood. However, only about half as much nitrous oxide was found in the fetal as in the maternal blood.

8. Judged by biochemical data, cyclopropane as an obstetrical anesthetic would appear to be perhaps less safe for the infant than the clinical appearance of the mother would indicate.

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MERCURIC CHLORIDE, POTASSIUM MERCURIC IODIDE, AND HARRINGTON'S SOLUTION IN SKIN DISINFECTION

Behavior and Uses

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BRIEF reference was made in a recent communication (27) to the remarkable effects produced when mercuric chloride, potassium mercuric iodide, and Harrington's solutions are applied to healthy skin. These phenomena were first observed when the germicides in question were subjected to a new quantitative test of skin disinfectant value (28). The purpose of the present paper is to report results of that work more fully, and on the basis of those findings and our interpretations of them to indicate what we consider to be the rational use of these widely employed disinfectants, and the place they should occupy in surgical technique.

The three germicides are combined in a single report because they are related chemically, and also because on skin they exhibit marked similarities in behavior.

Few drugs are more familiar to surgeons or have been more widely employed in surgery than these time-honored mercurials. Yet none has been less perfectly understood.

Bichloride of mercury was at the beginning of our modern surgical era given first place among antiseptics by Koch and other influential investigators (18, 24, 32, 34). Despite well known disadvantages, like irritation of tissues, precipitation of proteins, and corrosion of metals, the disinfectant soon became universally popular. Geppert (8) discovered, however, by precipitation of the mercury as an inert sulphide, that sublimated bacteria may still be alive though unable to grow in culture media, and that the action of the mercuric salt is bacteriostatic more than bactericidal. Halsted (10), Welch, and Kelly, applying this discovery clinically, demonstrated that although hands washed in bichloride may to ordinary tests appear nearly or quite sterile, subsequent use of ammonium sulphide shows them to be laden still with living bacteria—a phenomenon which has never been satisfactorily explained. Rodewald proved that certain bacteria, incapable after sublimation of growth in culture media, may yet be pathogenic when injected into the body. But these are only high lights. The disinfectant action of mercuric chloride has been the subject of literally countless investigations during the last 60 years. The trend, however, has been away from a study of the agent as a practical germicide to laboratory researches into the nature of disinfection (3, 14, 17, 21, 31, 33).

Potassium mercuric iodide, generally given a disinfectant rating approximately equal to that of bichloride, is believed to possess in addition certain important advantages—non-irritation of tissues, non-precipitation of proteins, and non-corrosion of metals. It has not been studied as intensively, however, or as critically as has bichloride. Most investigators of "biniodide"[1] have erred in failing to employ an antidote in their tests. Accepted uncritically, potassium mercuric iodide has become increasingly popular as a disinfectant for hands and for the field of operation.

Harrington's solution was introduced in 1903. It is perhaps the best known of many combinations of alcohol and mercuric chloride that have been recommended. It is conceded to be strongly germicidal, but an irritating quality has limited its practical usefulness.

EXPERIMENTAL INVESTIGATION

A recently introduced method (28) has been used by means of which the effect of any

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[1]The term "biniodide" of mercury is convenient but somewhat misleading. Formerly it referred to mercuric iodide (HgI_2). Latterly it has come to be used loosely for the complex potassium mercuric iodide (K_2HgI_4), whose active ion is $HgI_4^{=}$.

cutaneous germicide can be measured quantitatively in terms of reduction of the existing bacterial flora. The method consists essentially in (a) scrubbing the hands and arms in a perfectly uniform manner and for equal lengths of time in a series of basins of sterile water; (b) application of the germicide, followed (if desired) by its antidote; and (c) scrubbing as before in a second series of basins. Cumulative totals of bacterial counts of the washings (steps a and c) plotted against time produce curves from which the size of the bacterial flora of the entire cutaneous surface washed can be determined numerically. Comparison of the two curves, which are plotted independently, shows what effect the chemical has had upon the existing flora. Details of a typical experiment are given in Table I.

The solutions tested were: 1:1000 mercuric chloride, 1:500 potassium mercuric chloride, and Harrington's solution made up according to the original formula. These solutions were in every case freshly prepared from chemically pure salts and distilled water, were placed in sterile basins, and were used at 25 degrees C. without friction. Five or 10 per cent pure (light) ammonium sulphide solution proved a satisfactory antidote, controls showing that these strengths have of themselves no appreciable effect upon the cutaneous bacterial flora.

To recount all of our tests in detail would be tedious; instead results of groups of experiments will be reported, with illustrative figures and brief comments. The figures will repay careful study, since they show graphically what actually happened to the bacterial flora of the skin during these experiments, and indicate what occurs whenever a surgeon washes his hands in one of these mercurials.

1. Effects of applying mercuric solutions to skin. The actions of the three germicides are quite similar. Used for one minute or longer, the invariable result is that very few bacteria, either normal or sublimated, can be found in the second series of basins; i.e., a cutaneous surface is produced which yields few if any organisms when washed and brushed. Figure 1 shows how the total flora of the hands and arms, which was being reduced at a regularly logarithmic rate by scrubbing (in the first series of basins), became fixed, as it were, at that level by the mercurial so that subsequent scrubbing failed to reduce it further. When, however, as in Figure 2, the mercurial is followed by an antidote, results are quite different, for the second period of scrubbing in that case reduces the flora at the same rate as the first. These characteristic effects—fixation of the cutaneous bacteria and their release—are illustrated even more clearly in Figure 3. This is precisely the phenomenon described 50

TABLE I.—EFFECTS OF 1:500 POTASSIUM MERCURIC IODIDE SOLUTION UPON THE BACTERIAL FLORA OF HANDS AND ARMS.

Basin	Scrubbing time	Total bacterial count for basin	Cumulative totals washed off	Actual totals, or size of flora left
	minutes	organisms	organisms	organisms
				7,663,690 (a)
1	2	2,894,780	5,913,690	4,768,910
2	1	784,420	3,108,910	3,984,490
3	1	460,500	2,234,490	3,524,990
4	2	786,980	1,774,990	2,738,010
5	2	525,760	988,010	2,212,250
6	2	462,250	462,250	1,750,000 (b)
At this point hands and arms washed in 1:500 K_2HgI_4 solution for 60 seconds. Temperature 24.5 C. Excess of disinfectant quickly rinsed off and scrubbing resumed.				
				1,750,000 (c)
7	1	3,000	24,730	1,790,000 (d)
8	2	10,900	21,730	1,860,000 (e)
9	2	6,450	10,830	1,950,000 (f)
10	2	4,380	4,380	2,046,000 (g)
Hands and arms washed in 5 per cent $(NH_4)2S$ solution for 1 minute. Excess rinsed off, and scrubbing resumed in a third series of basins.				
				2,046,000 (h)
11	2	216,250	1,146,000	1,829,750
12	2	337,550	929,750	1,492,200
13	2	386,400	592,200	1,105,800
14	2	205,800	205,800	900,000 (i)

(a) Total number of bacteria on the hands and arms at the beginning of the experiment; (b) after 10 minutes of scrubbing; (c) after use of the disinfectant; (g) after the second period of scrubbing (7 minutes); (h) after using the antidote; and (i) after the third period of scrubbing (8 minutes). (b) and (i) are arrived at by mathematical projection of the curves to zero. (c), (d), (e), (f) and (g) are estimated from the known curve values and the cumulative totals of bacteria washed off in the second group of basins.

Control cultures made of water, glassware, media, air contamination, etc. Special tests showed that washings in basins 7 ard 11 were not bacteriostatic. Previous tests had shown that neither potassium mercuric iodide nor ammonium sulphide solutions kill appreciable numbers of bacteria when applied to skin.

Actual totals of this experiment, plotted against time, are shown in Figure 3.

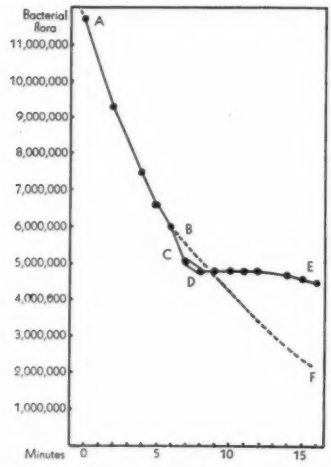

Fig. 1. Results of washing in 1:1000 mercuric chloride without a neutralizing agent. *AB*, Effect of scrubbing for 6 minutes; *BC*, increased effect, due to scrubbing for 1 minute without soap; *CD*, relatively slight reduction of total flora caused by washing for 1 minute in the mercurial at 25 degrees C.; *DE*, result of subsequent period of scrubbing.

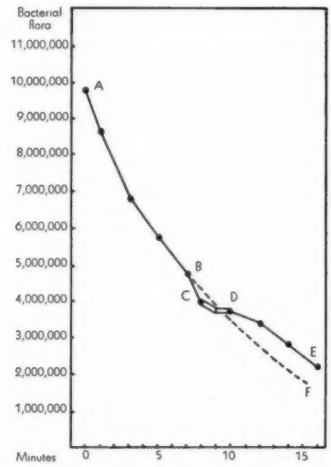

Fig. 2. Results obtained when the mercurial is followed immediately by its antidote. *ABC*, Reduction of flora during the first period of scrubbing, the last minute of this without soap; *CD*, hands and arms washed in 1:1000 mercuric chloride for 1 minute, followed by ammonium sulphide solution; *DE*, indicates the second period of scrubbing.

years ago by Halsted, Welch and Kelly, but which has never been satisfactorily explained.

Other experiments of a similar nature have brought out additional facts. If hands which have been washed in a mercurial and in consequence present a germ-free surface are scrubbed long and vigorously enough, bacteria begin to appear in the washings, until at length (after 20 minutes of scrubbing in one of our experiments) bacteria may come away at the usual rate. A biniodide surface is found to be more resistant to such friction than one produced by bichloride. Furthermore, the number of cutaneous organisms killed by washing the hands and arms in potassium mercuric iodide or Harrington's solutions is very small—too small, indeed, to be detected by our quantitative test. Mercuric chloride has a slight bactericidal effect, reducing the total flora by about 5 per cent per minute, which is about half the rate of degermation by scrubbing. Even this slight action diminishes after a few minutes' exposure to the chemical, and eventually ceases altogether, so that further soaking in the disinfectant is without bactericidal effect.

To explain these results we postulate a combination of some sort between the epidermis and mercuric salt to produce, in effect if not actually, a thin, transparent film which covers the cutaneous surface and its minute crevices and depressions wherein lie most of the bacteria (28). This interaction takes place so rapidly, especially in the case of potassium mercuric iodide and Harrington's solution, that the "film" prevents the germicides from coming into effective contact with the underlying bacteria. In other words, on skin the germicidal activity of all three of these agents is self-limiting to a remarkable degree. These "films" can be abraded by prolonged brushing, in consequence of which some of the underlying organisms are released. Ammonium sulphide, on the other hand, acts upon the "film" chemically, so changing its character that it no longer hinders removal of bacteria from skin at the usual rate.

2. *The fate of bacteria beneath the "film."* The experiments here described indicate clearly that skin organisms held momentarily under these "films" are alive, and upon escape are fully capable of growth in culture media.

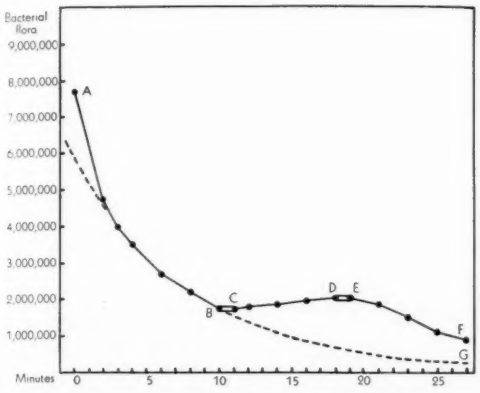

Fig. 3. Results obtained when the mercurial is followed by a delayed use of the antidote. *AB*, Results of the first period of scrubbing; *BC*, 1:500 potassium mercuric iodide washed in for 1 minute, followed by a second period of scrubbing, *CD*; 5 per cent ammonium sulphide applied, *DE*, and scrubbing was resumed in a third series of basins.

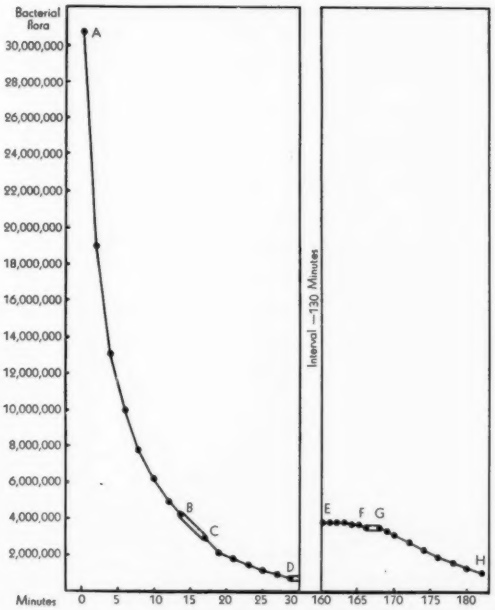

Fig. 4. Bacteriological effects of wearing the "film" for a longer period of time. The very large initial flora in this instance was the result of having washed in a mercurial and its antidote a few days previously. Prolonged scrubbing, *AB* and *CD*, and 3 minutes application of 60 per cent by weight (approximately 70 per cent by volume) alcohol, *BC* reduced the bacterial count to 705,000. *D*, Hands and arms washed in 1:500 potassium mercuric iodide solution. During 130-minute interval skin not protected from clothing or other unsterile objects in laboratory; *EF*, scrubbing resumed; *FG*, ammonium sulphide applied; *GH*, final period of scrubbing.

A second group of experiments was designed to study the effect of longer periods of imprisonment. In these tests the flora of the hands and arms were first measured, in some cases qualitatively as well as quantitatively; then the mercurial was applied; finally after selected periods of time the "film" was broken-up by ammonium sulphide and friction, and the flora measured anew. The following effects were observed.

Beneath these "films" bacteria of the skin not only live uninjured, but proceed at once to multiply at an abnormally rapid rate, their number doubling every 55 to 60 minutes. Generation time on skin ordinarily is several hours (28). Figure 4 shows that the increased flora comes away with scrubbing at the same rate as the original flora. Furthermore, our qualitative studies provided evidence that the different sorts of bacteria which make up the cutaneous flora all participate in this increase, and apparently at much the same rate.

The effect of "films" upon underlying bacteria over much longer periods of time was noted also. As might be expected, unlimited increase in numbers of organisms is counteracted by gradual break-up of the "films" by friction against clothing and other objects, with consequent loss of surplus bacteria from the skin. Figure 5 shows conditions found 3 days after the hands and arms had been washed in bichloride without an antidote. A rather large flora was encountered, and enough of the "film" remained to interfere considerably with degermation by scrubbing.

Strangely enough, when hands have been washed in one of these mercurials, followed immediately by ammonium sulphide, their bacterial counts may, in a few days, reach 15 to 30 million or more. These large bacterial populations are reduced by scrubbing at the same rate as the ordinary flora of skin.

It has been shown (28) that cutaneous bacteria are ordinarily of two sorts—"resident" and "transient" (contaminating) organisms. The latter are much more easily killed or removed than the former. Since well scrubbed

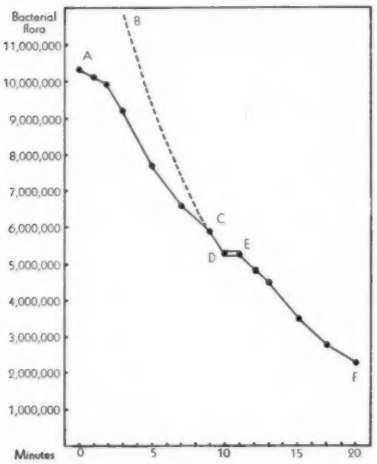

Fig. 5. The bacterial flora 3 days after the hands and arms had been washed in 1:1000 bichloride solution without a neutralizing agent. *A*, Initial flora; *CD*, effect of brushing without soap; BC, usual rate of degermation by scrubbing; *DE*, 30 per cent ammonium sulphide applied.

hands are virtually free from contaminating germs, all the foregoing observations are concerned with the "resident" flora. It is of importance, however, to know what effect these disinfectants have upon contaminated hands. Consequently, experiments were performed in which known numbers of identifiable test bacteria, not normally found on skin, were rubbed on the hands, which then were washed in bichloride or "biniodide" solution. After various intervals of time an antidote was applied and the skin was tested, quantitatively and qualitatively, for surviving organisms. These experiments were not wholly successful. Technical difficulties were encountered in adapting differential culture media to quantitative studies. And perhaps certain variables, like the thoroughness with which the test-bacteria were rubbed on the skin, were not controlled carefully enough. But at least this significant result may be reported: In none of these tests did the disinfectant kill all the contaminating organisms, whereas under the "film" the remainder multiplied until, in some instances, they at length exceeded the original number.

3. Impermeability of the "film." It has been noted already that the outer surfaces of these "films" remain sterile, or very nearly so, even though the skin beneath may harbor large numbers of "resident" and contaminating bacteria. This strongly suggests that the film-like structure does not permit passage of bacteria. Corroboration was provided by experiments in which test organisms were placed on the outside of the "film." After given intervals of time, the "film" was carefully washed off and treated with ammonium sulphide. None of the test organisms could be found on the skin beneath.

Permeability of the "film" to alcohol was tested also. It has been shown elsewhere (27, 29) that a solution of alcohol exactly 70 per cent by *weight* is a very effective skin disinfectant. When skin is washed without friction for 2 minutes in this solution, its bacterial flora is reduced by about 76 per cent. We found, however, that if the hands are first bathed for a minute in 1:500 potassium mercuric iodide solution, 70 per cent alcohol is capable of reducing the flora by only 15 per cent, doubtless because the "film" prevents the alcohol from making effective contact with the bacteria of the skin. Harrington's solution contains 60 per cent (by volume) alcohol and 2 per cent hydrochloric acid, both of which are somewhat germicidal on skin as well as *in vitro*. But Harrington's solution kills a negligible number of organisms when applied to skin, in all probability because the mercuric salt acts promptly to form a "film" which protects the underlying bacteria from the other chemical agents.

4. Chemical nature of the "film." It is commonly stated that mercuric chloride reacts with the proteins of skin to form mercuric albuminate, and that addition of ammonium sulphide precipitates the mercury in the form of mercuric sulphide as proved by discoloration of the skin. That, however, is oversimplification of a very complex set of changes.

Even in the case of soluble albumins the problem is complicated as the following simple test tube experiments indicate.

1. Interaction between mercurial and soluble albumin.

$HgCl_2$+ascitic fluid→a white precipitate

This precipitate, probably a mercuric proteinate of some sort, settles in light flocculent form, leaving a clear supernatant fluid which seems to contain both

mercury and protein, however, since it turns amber-colored upon addition of sulphide (see interaction *3*). The precipitate dissolves in an excess of ascitic fluid.

2. Interaction between mercurial and sulphide.

$HgCl_2 + (NH_4)_2S \rightarrow HgS \downarrow + 2\ NH_4Cl$

This is a heavy black granular precipitate which settles rapidly, especially after several washings.

3 and 4. Interactions between the "mercuric proteinate" and sulphide.

3. White precipitate (from 1) + $(NH_4)_2S$ → a brown precipitate.

This is a dirty-brownish flocculent precipitate which settles slowly at first, but more rapidly when washed. It does not look like the mercuric sulphide (HgS) of *2*. It dissolves readily in an excess of sulphide, imparting an amber color to the solution. The presence of a relatively small amount of ascitic fluid suffices to prevent formation of the black mercuric sulphide (HgS) in *2*.

4. White precipitate (from 1) + a large excess of $(NH_4)_2S$ → a blackish precipitate.

All four of these interactions are practically instantaneous.

Solubilities of the precipitates are as follows:

Solvent	*1*	*2*	*3*	*4*
Water	o	o	o	o
Alcohol, 70 per cent (by weight)	o	o	o	o
Sodium chloride, saturated solution	o	o	o	o
Hydrochloric acid, N/10	±	o	±	o
Acetic acid, 14 per cent	±	o	±	o
Sodium hydroxide, N/10	o	o	o	o
Excess of ammonium sulphide		o	±	o
Potassium iodide solution	+	o	±	o

Obviously the result of interaction *3* is not simply to precipitate mercuric sulphide. There we are dealing with complex actions between organic and inorganic substances.

What happens on skin, especially when a great excess of ammonium sulphide is not employed, is difficult to determine. Here the problem is complicated by the fact that we are concerned, not with soluble albumins, but with albuminoids which are characterized by insolubility. So also, doubtless, are their compounds. The discoloration of skin produced by mercuric chloride cannot be removed with acids or potassium iodide.

As for potassium mercuric iodide, it is generally held that this reagent does not precipitate albumin nor react with the skin. Against such a view it may be pointed out that the presence in solution of egg or serum albumin diminishes the bactericidal activity of potassium mercuric iodide, even though no visible precipitation takes place; that the salt does "combine" with skin, as we have shown and that this combination is in turn acted upon by ammonium sulphide; and that although hands washed in potassium mercuric iodide solution will not be stained by 5 or 10 per cent ammonium sulphide, they will be turned black by 30 per cent solution.

The following simple test is also significant: If to an aqueous solution of potassium mercuric iodide a little ammonium sulphide is added, a clear amber-colored solution results. If more ammonium sulphide is added, a black precipitate appears[2] which is insoluble in all ordinary reagents. This action is non-reversible. In an alcoholic, and especially an acetone, solution of potassium mercuric iodide the precipitate appears sooner; but the presence of serum albumin in the solution delays its appearance.

It appears, therefore, that potassium mercuric iodide "reacts" with, or is absorbed by, albumin, but that the compound or complex remains in solution or suspension; that the mercuric salt also "reacts" with the albuminoids of the skin to form a colorless complex that is not acted upon by water; that small amounts of ammonium sulphide act upon these complexes, changing them but not producing any visible precipitate; and that a great excess of ammonium sulphide acting upon either complex produces a black precipitate, which is at least very similar to mercuric sulphide.

The reason, probably, why use of potassium mercuric iodide (without an antidote) does not turn nails and skin dark is that the amount of mercuric mercury free to combine with the sulphur compounds of skin is infinitesimally small.

EVALUATION OF STUDY

The production of an invisible, sterile, impermeable "film" whenever non-greasy skin is washed in one of these mercurials—a "film" which overlies and protects the cutaneous bacteria, and may be destroyed with difficulty by friction but easily by means of an alkaline sulphide—is, we believe, the true explanation of the phenomenon which so puzzled Halsted and Welch. It is perhaps the chief reason why certain surgeons, in days before rubber gloves came into use, were able at times to

[2]For further discussion of reactions between mercuric salts and alkaline sulphides see Mellor, J. W.: A Comprehensive Treatise on Inorganic and Theoretical Chemistry. London and New York: Longmans, Green & Co., 1923, IV, 828 and 944.

operate bare-handed with almost perfect asepsis. And it helps to explain why various investigators, testing the skin-disinfectant value of these mercurials, using different technique, should have obtained such divergent results.

The following is an attempt to indicate the rational and most effective use of these mercurials, and the place which they should occupy in surgical technique. The recommendations are founded upon the experimental studies outlined in this paper, but they have also been tested practically over a period of 3 years in the University Hospital (Tsinan, China) with clinical results which strengthen our belief in their truth and value.

In pre-operative disinfection of hands bichloride and "biniodide" of mercury should have a definite though limited place. When for any reason the ungloved hand must be used in surgery or obstetrics, one of these agents may be employed to great advantage. A solution of 1:500 potassium mercuric iodide is the preferable one. Short nails, a thorough preliminary scrub, followed by a one-minute wash in the mercurial, and the operator will have on his hands the equivalent of an invisible, extremely thin but strong, sterile glove. That procedure will also increase the margin of safety for the occasional operator, even though he wears rubber gloves. But neither bichloride nor "biniodide" is recommended for constant use. Hands which have been washed recently in any of these mercurials may be expected to have abnormally large bacterial counts which cannot be reduced easily or with any certainty. If it is desired to use both alcohol and a mercurial, the former to be effective should precede, not follow, the latter.

In preparation of the field of operation also, potassium mercuric iodide should have a well understood place. Applied to non-greasy skin, this agent produces a surface which is practically germ-free and probably will remain so throughout the operation, provided it is not abraded unduly. But any incision must of necessity pass through the "film" and the germ-laden skin beneath, inevitably inviting infection of the wound. If, however, the site of incision is first adequately degermed—methods of accomplishing this have been described (27, 29)—a mercurial may then be used effectively to disinfect the surrounding area of skin, in the sense of walling-off all the nearby potentially infectious bacteria. Such a procedure is particularly useful in treating large irregular surfaces, such as the hand or foot, which are difficult to "paint" with a germicide but are easily soaked for a minute or more in a basin of potassium mercuric iodide solution.

Use of bichloride or "biniodide" solutions to disinfect hands contaminated with pathogenic micro-organisms is contra-indicated. It cannot be expected that all the infectious bacteria will be killed thereby. The pathogenic germs that remain alive may multiply, some to escape as the "film" is abraded, others to be incorporated gradually into the "resident" flora of the skin. It is conceivable that hands may thus become both acute and chronic healthy carriers of infection.

Since Harrington's solution is shown to possess no advantages over bichloride and "biniodide" solutions, but has the disadvantage of being irritating to skin, its use might well be abandoned altogether.

SUMMARY

1. The skin disinfectant properties of mercuric chloride, potassium mercuric iodide, and Harrington's solutions have been investigated, by means of a recent experimental method which tests quantitatively the degerming action of disinfectants upon skin.

2. The three solutions are quite similar in behavior when applied to skin. Strictly speaking, they are disinfectants rather than germicides, the reason being that they reduce the bacterial flora of normal skin very slightly or not at all; yet all three are capable of producing a sterile, or nearly sterile, skin surface. This is due to "reaction" of the mercurial and epidermis to form a film-like structure which overlies the bacteria.

3. This invisible "film" is impervious to bacteria, is only slightly permeable to alcohol, and is remarkably resistant to friction.

4. Beneath the "film" cutaneous bacteria not only live unharmed, but multiply at an abnormally rapid rate, their number doubling every 50 to 60 minutes.

5. The "film" may be abraded by prolonged friction, and the underlying bacteria then slowly liberated. Ammonium sulphide, on the other hand, acts upon the "film" promptly, destroying it (at least in its original form), so that subsequent removal of skin organisms is not interfered with.

6. The complex chemical reactions involved are discussed.

7. On the basis of our experimental results, the following recommendations are made as to the rational use of these disinfectants in surgery:

8. Harrington's solution might well be discarded altogether.

9. Bichloride and "biniodide" of mercury have a definite though limited place in preoperative preparation of hands. They should not be employed routinely or frequently, but in lieu of rubber gloves and for the occasional operator, their use seems clearly indicated.

10. They have a value also in preparation of the field of operation, provided the site of incision is first adequately degermed.

11. Neither solution should be used to disinfect hands contaminated with pathogenic bacteria.

12. These recommendations have been tested clinically with satisfactory results.

It is a pleasure to express my indebtedness to Dr. J. Howard Brown for generously granting me facilities of his laboratories, and for helpful suggestions in preparation of this material for publication. I am under obligations also to Dr. Leslie Hellerman for constructive criticism of the chemical aspects of this report.

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THE MAINTENANCE OF LIFE DURING EXPERIMENTAL OCCLUSION OF THE PULMONARY ARTERY FOLLOWED BY SURVIVAL

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THE remarkable advances made in thoracic surgery in recent years have been accompanied by progress in surgery of the heart. The experimental demonstration of the nature of Pick's disease (2) and its operative cure (2, 4, 19, 20) constitute a past chapter in the history of cardiac surgery. The repair of wounds of the heart is being accomplished with an increasingly lowered mortality rate (8). Recently a method of establishing a collateral blood supply for the myocardium when the coronary vessels become occluded has been demonstrated upon animals (3, 16) and applied successfully to patients (1). However, attempts to carry out surgical procedures within the cardiac chambers or great vessels at the base of the heart have not been attended as yet with much success. The Trendelenburg operation of pulmonary embolectomy is associated with a discouraging mortality (14) and has not yet been successfully accomplished in this country. Surgical procedures designed to relieve a stenosis of the mitral valve have been even less successful (5).

It is obvious that any operative procedure upon the heart could be performed better if that organ were temporarily relieved of its function of pumping blood. For example, if the flow of blood through the heart and lungs could be safely stopped for 30 minutes, it is conceivable that a new field of cardiac surgery might be developed.

In order to maintain life during such a temporary cessation of blood flow through the heart and lungs, it is necessary to assume the functions of these organs by some other means. This might be accomplished, as suggested by Phemister, by continuously injecting arterial blood from a number of suitable donors into the arterial system of the patient, while at the same time continuously withdrawing venous blood from the patient and injecting that venous blood into the same donors. The complexities of such a procedure and the difficulties of obtaining a number of individuals willing to undergo the procedure are apparent. Obviously it would be more desirable to assume the functions of the heart and lungs temporarily by a mechanical apparatus. Some of the difficulties and complexities would still be present; but if they could be overcome, the advantages of such a mechanical apparatus are easily seen.

The problem which presented itself to us was largely one of adapting one or more of the various perfusion methods which have been used in the past in the study of isolated organs. Indeed, there would be no problem at all except that of the increase in size of the apparatus, if large tubes could be tied into the aorta and into the vena cava, as is done with the main artery or vein of an isolated organ. However, if the functions of the heart and lungs are assumed only temporarily by a mechanical apparatus, these large vessels cannot be divided and ligated for cannulation. The perfusion must be carried out through smaller peripheral vessels. Oxygenated blood must reach the aorta by a reverse flow through one or several peripheral arteries. These arteries must be so small that after removal of the perfusing cannulas, their ligation does not entail any damage to the peripheral tissues which they supply. Perhaps if a sufficient number of small arteries were used, the vessels might be punctured with needles and heal without requiring ligation.

Similarly, a rapid free flow of venous blood must be obtained from the main venous reservoirs of the body by way of one or more peripheral veins. Veins must be employed in

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which no valves are interposed between the point of needle puncture or cannulation and the large intrathoracic veins. Here an additional problem presents itself in that a much more rapid flow of blood must be established through small vessels with collapsible walls than obtains under normal circumstances. Thus, unless a relatively enormous number of peripheral veins without valves are employed for needle puncture the walls of the veins so used will collapse. A simpler method is to use a rigid walled cannula. The cannula must be of such a bore that it may be inserted into a small peripheral vein, and must be long enough to reach a vein of large caliber, where the flow of blood will not be so rapid as to induce collapse of its walls. On withdrawal of the cannula the vein may be ligated. This requirement for using small arteries and small veins for the perfusion increases the difficulties of the procedure, and constitutes the only essential difference between perfusion of isolated organs and the temporary assumption of the functions of the heart and lungs of a whole animal.

The successful assumption of the functions of the heart and lungs of an animal by purely mechanical means and by the use of small peripheral vessels, has already been described (9). However, in only 3 instances were the animals able to resume their normal cardiorespiratory functions after the period of perfusion. In these 3 animals the pulmonary artery was completely occluded, hence the flow of blood through the heart and lungs completely stopped for periods of 30, 33, and 39 minutes. During the period in which the pulmonary artery was occluded, life was maintained by perfusion of the animal through a small artery and a small vein. The pulmonary artery was then released, thus allowing blood once more to flow through the heart and lungs, and the perfusion was stopped. None of these animals survived for more than 4 hours after the perfusion had been stopped. The present communication deals with further development of this method and reports prolonged survival after short periods of temporary occlusion of the pulmonary artery.

Many excellent devices have been described for pumping blood through a perfusion circuit. The one which was thought to be most suitable for our purpose was that described by Dale and Schuster, the essential feature of which is a rubber finger cot which is alternately compressed and expanded by air. Such a pumping arrangement requires the insertion of one-way valves in the blood circuit in order to direct the flow of blood. A modification of this Dale-Schuster pump was used originally (9). In the course of that work an article appeared by DeBakey describing a constant injection roller type of pump which he employed in blood transfusions. This pump eliminated the necessity for valves, and a modification of it driven by an electric motor has been adopted in the work here reported.

A great many methods for introducing oxygen rapidly into the blood have been developed in connection with the perfusion of isolated organs. Their chief disadvantage for use in our problem was that they all required a large quantity of blood in relation to the surface area afforded for oxygenation. Consequently, in the work reported earlier (9) and in the present report an oxygenator has been used which has a large surface-volume ratio (10). It was designed expressly for use in this work. It has this added advantage that there is little or no trouble with frothing or foaming, an undesirable feature often present in other oxygenators which have been described.

APPARATUS

The procedure employed was essentially similar to that previously reported (9). Venous blood was withdrawn from the superior vena cava through a cannula in the right jugular vein, oxygenated, and reinjected through a cannula in the right carotid artery in a central direction.

The apparatus used to oxygenate the blood has already been described (10). The essential features are indicated diagrammatically in Figure 1, and the apparatus is shown in Figure 2. The stream of blood is directed against the inner surface of a rapidly revolving cylinder, *A*, where it is spread into a thin film by centrifugal force. This film moves downward by gravity and is collected in a stationary cup, *B*, at the bottom of the cylinder. The cup, *B*, is funnel shaped and the opening at the bottom is continuous with the lumen of a

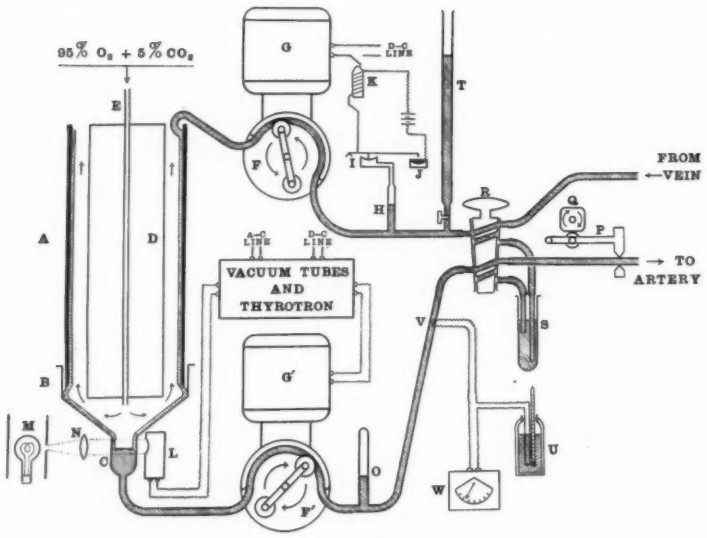

Fig. 1. Diagram, not drawn to scale, of the extracorporeal circuit used to withdraw venous blood, introduce oxygen, and return the blood to the arterial system. For description see text.

glass cup with vertical walls, *C*. Most of the space within the revolving cylinder, *A*, is occupied by a stationary cylinder, *D*. This cylinder, *D*, is closed at both ends except for a tube, *E*, which serves to convey a mixture of 95 per cent oxygen and 5 per cent carbon dioxide to the bottom of the oxygenator. This gas mixture is blown through the apparatus at the rate of 5 liters a minute and passes upward between cylinders, *A* and *D*, to escape at the top of the apparatus.

The blood is moved through the circuit by 2 pumps. The pump, *F*, transfers blood from the superior vena cava to the oxygenator. The pump, *F'*, returns the oxygenated blood to the animal's aorta through the centrally directed cannula in the right carotid artery.

The pumps used to move the blood through the circuit are of the constant injection roller type. The objection to these pumps has always been that the rubber tubes compressed by the rollers gradually move forward as the rollers pass over them. To avoid this "creeping," DeBakey employed rubber tubes with a projecting, flat, rubber flange. The flange is clamped between 2 semicircular metal bars. This device holds the tube firmly in position and prevents any forward movement as the rollers pass over and compress the tubing. This improvement of DeBakey was incorporated in the design of the pumps, *F* and *F'*, but is not indicated in Figure 1. Each pump accommodates 3 rubber tubes, arranged in a tier, one above the other. The 3 tubes are compressed simultaneously by each roller. The pumps are driven by shunt-wound one tenth horse power direct current electric motors, *G* and *G'*. The motors are geared to the pumps by speed reducers with a ratio of 20 to 1. The speed of the motors and thus the output of the pumps is controlled by a rheostat which varies the current flowing through the armatures of the motors.

If blood is withdrawn from the superior vena cava by the pump, *F*, more rapidly than it enters that vein from its tributaries, the wall of the vena cava is drawn against the opening of the cannula. Unless the pump is immediately stopped, the wall of the vein continues to be held in this position, and the extracorporeal circulation comes to an abrupt end. It was necessary to provide for an instantaneous ces-

sation of the sucking action of the pump, *F*, whenever this occurred. This was accomplished by introducing a vertical T-tube, *H*, between the pump, *F*, and the cannula in the jugular vein. The upper end of this T-tube is connected with a membrane manometer, *I*, which supports a lever above a small cup of mercury, *J*. When the tip of the lever comes in contact with the mercury, an electrical circuit is completed through a relay, *K*, which cuts off the current to the motor, *G*, driving the pump, *F*. With such an arrangement, whenever the wall of the vein occludes the tip of the venous cannula, the blood level in the T-tube, *H*, abruptly falls, lowering the air pressure in the membrane manometer *I*. By means of the relay, *K*, the current to the motor, *G*, driving the pump, *F*, is interrupted. The pump immediately stops, suction ceases, and the wall of the vena cava is drawn away from the tip of the cannula by the filling of the vein with blood. The level of blood in the T-tube, *H*, then rises, the above process is reversed, and the pump, *F*, resumes action. When such a sequence of events occurs it is an indication that the pump, *F*, is withdrawing blood from the vena cava more rapidly than blood is entering that vein. Hence the speed of the pump is decreased by reducing the current flowing through the armature of the motor, *G*. During the course of an experiment the intermittent action of the pump, *F*, produced by the above sequence of events, would occasionally go unnoticed. Therefore, a small electric bell was inserted in the relay circuit. This is not indicated in Figure 1. When the bell rings, the operator knows that the speed of the pump, *F*, should be reduced.

It is essential that the output of the pump, *F'*, correspond exactly to the amount of blood entering the cup, *C*, at the bottom of the oxygenator. If blood is pumped from the cup, *C*, more rapidly than it enters, the level of blood in the cup falls and air bubbles are drawn into the tubing and so driven into the animal's artery with resultant arterial air embolism. On the other hand, if the pump removes blood from the cup, *C*, more slowly than blood enters from the oxygenator, there is a gradual accumulation of blood in the cup with resultant depletion of blood in the animal's vascular system. This produces a fall in blood pressure and proves as disastrous as air embolism. These difficulties could not be overcome by driving both pumps, *F* and *F'*, at the same speed, because small variations in the diameter of the tubes compressed by the pumps, or differences in the resistance offered to the outflow or the inflow of either pump would still produce an inequality in output between the 2 pumps. Hence it was essential that the output of the pump, *F'*, be regulated solely and completely by the level of the blood in the cup, *C*, at the bottom of the oxygenator.

It is possible to regulate the output of the pump, *F'*, by hand so that the level of blood in the cup remains constant and neither of these undesirable and often fatal events occur. However, this requires the undivided attention of one assistant during the whole period of perfusion, and the slightest relaxation of attention on his part may result in the death of the animal. A more satisfactory and completely automatic control of the pump, *F'*, was obtained by using a photo-electric cell, *L*, vacuum tube amplifiers, and a thyrotron tube.[1]

The photo-electric cell, *L*, is placed behind the glass cup, *C*, at the bottom of the oxygenator. A strong beam of light from a 100 Watt bulb, *M*, is concentrated by a lens, *N*, and directed through the glass cup to the photo-electric cell, *L*. The current from the photo-electric cell is amplified by 2 vacuum tubes in series. The amplified current saturates a reactor, which in turn shifts the phase of the alternating current grid voltage with respect to the alternating current plate voltage, resulting in varying plate current from the thyrotron. This plate current then flows through the armature of the shunt-wound direct current motor, *G'*, geared to the pump, *F'*. A rise in the level of the blood in the cup diminishes the amount of light reaching the photo-electric cell and produces an increase in the speed of the electric motor driving the pump, *F'*. Conversely, when the level falls, more light reaches the photo-electric cell and the output of the pump, *F'*, is diminished. With this arrangement the level of the blood in the cup does not vary more than a few millimeters even with wide

[1] I am indebted to Dr. Carl C. Chambers, of the Moore School of Electrical Engineering of the University of Pennsylvania for designing this electrical circuit.

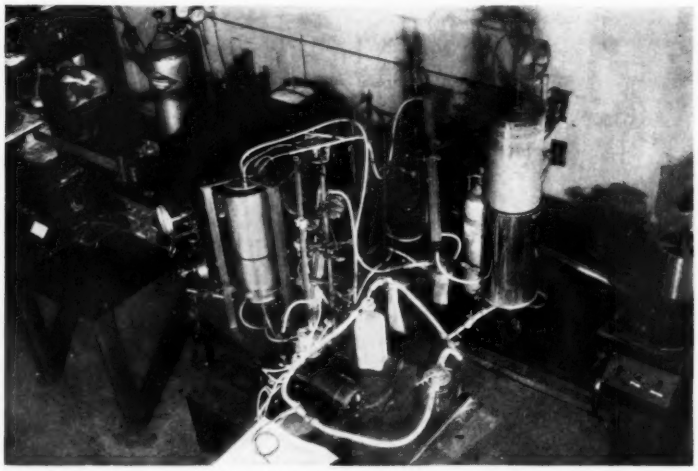

Fig. 2. Photograph of the apparatus, showing in the center the revolving cylinder of the oxygenator and the 2 blood pumps. To the left are vacuum tube amplifiers and thyrotron, and to the right the closed oxygen rebreathing circuit connected with a bell spirometer filled with oxygen.

variations in the output of the pump, *F*. When the pump, *F*, stops, the pump, *F'*, stops also, always maintaining the same level of blood in the cup, *C*, at the bottom of the oxygenator.

The flow of blood on the output side of the pumps is not perfectly smooth. Slight pulsations are produced each time the rollers begin or cease to compress the tubing. The rate of these pulsations varies with the output of the pumps, being more rapid as the output increases. Thus at the slowest speed there are 6 pulsations a minute, and at the highest 220. A pulsatile pressure in arteries has been shown to be essential to the normal function of organs (13). However, the wide variations in pulse rate occurring with variations in the output of the pumps were thought to be undesirable. Therefore, the pulsations from the pump, *F'* are eliminated by introducing a T-tube, *O*, with a long, wide upright portion into the circuit just beyond the pump, *F'*. The end of the vertical limb of the tube is closed. This air cushion eliminates pulsations and gives an almost smooth flow. A pulsatile flow into the carotid artery is produced by a horizontal bar, *P*, which compresses the tubing leading to the arterial cannula at the rate of 150 times a minute. This approximates a cat's heart rate under ether anesthesia. The intermittent compression of the tubing is accomplished by the revolution of a square wheel, *Q*, with rounded corners which forces the bar downward across the tubing 4 times with each revolution. The wheel is geared to an electric motor so that the rate of the pulsations in the tubing can be adjusted to the desired speed.

It is essential to maintain a constant volume of blood in the animal's vascular system. To do this it is necessary to start withdrawing blood from and injecting blood into the animal at the same instant and at the same rate. This is accomplished by passing both venous and arterial blood through the same stopcock, *R*. The stopcock contains 4 internal channels, 4 outlets on one side and 2 outlets on the other side. With the stopcock, *R*, in the position shown in Figure 1, the extracorporeal circuit is connected with the tubes leading to the arterial and venous cannulas, and in the reverse position the circuit is connected with 2 tubes entering a small test tube, *S*. Prior to perfusing the animal, the extracorporeal circuit is filled through the burette, *T*, with heparinized blood previously obtained from another cat. This blood is then slowly moved around the circuit by the pumps with the oxy-

genator cylinder, *A*, revolving. The blood is pumped from and into the small test tube, *S*. The purpose of this is to stabilize temperature conditions throughout the circuit. When the operative procedures in the animal are completed, a single half turn of the stopcock, R, connects the extracorporeal blood circuit with the animal's own circulation. The circuit itself is so devised that it always holds a very constant volume of blood, due in large part to the photo-electric cell control of the pump, *F'*. By these means it is possible to maintain a constant volume of fluid in the animal's vessels.

The blood is maintained at body temperature during its passage through the extracorporeal circuit by surrounding as much as possible of the apparatus with a moving stream of warm water. For the sake of simplicity this water jacket is omitted from Figure 1. Three portions of the blood circuit are surrounded by the water bath. Between the glass stopcock, *R*, and the pump, *F*, the blood passes through a glass tube in a Leibig condenser. The stationary cup, *BC*, at the bottom of the oxygenator consists of 2 portions: The upper part, *B*, is of metal and has a double wall; the small, lower portion of the cup, *C*, is of glass and also has a double wall. Warm water is continuously circulated through the Leibig condenser and between the walls of the stationary cup, *BC*, in both its metal and glass portions.

In addition to this warming of the blood circuit, the cold dry gas from a cylinder of 95 per cent oxygen and 5 per cent carbon dioxide is warmed by passing it through a spiral tube immersed in the warm water reservoir. The gas is then saturated with water vapor by bubbling it through the warm water. To prevent condensation the warm gas saturated with water vapor is passed through warm tubes until it enters the oxygenator. Water is pumped to and from a 4 gallon water reservoir through the water jacket at the rate of 850 cubic centimeters per minute. The water bath is heated by a 500 watt knife-type immersion heater. The temperature is controlled by a thermostat inserted into the water bath which, acting through a relay, controls the current to the knife heater. The thermostat maintains the temperature of the water bath within a plus or minus 0.5 degree C.

The animal's rectal temperature, the temperature of the blood passing through the circuit, and the temperature of the water bath are recorded at 3 minute intervals during the course of an experiment. Thermocouples are used instead of mercury thermometers, because of the rapidity with which they follow fluctuations of temperature and, in the case of the blood circuit, because it was simpler to insert a small wire in the blood stream than it was to immerse the large bulb of a mercury thermometer. All 3 temperatures can be read by an assistant at some distance from the operative field and the apparatus, a consideration of some importance when the operations are performed under sterile conditions. Copper constantan junctions are used for thermocouples, the control junctions are placed in a thermos bottle, *U*, containing mineral oil and the testing junctions are inserted into the animal's rectum, the blood circuit, *V*, and the water bath circuit, respectively. The readings are made on a scale at a distance of 1 meter from a mirror-type d'Arsonval galvanometer, *W*. The external resistance for critical damping is placed as a shunt across the galvanometer posts and a suitable resistance is placed in series with the thermocouples so that a deflection of 1 millimeter of the hair line on the scale corresponds to a change of temperature of 0.1 degree C. With water at a temperature of 39.5 degrees to 40.0 degrees C. circulating through the 3 jackets described, the temperature of the blood in the circuit is maintained at approximately 38.5 degrees C. Under these circumstances the rectal temperature is maintained at 38.0 degrees C. or above.

The extracorporeal circuit, with the oxygenator cylinder, *A*, revolving, holds 65 cubic centimeters of fluid. The fluid is distributed as follows: 35 cubic centimeters on the inside of the revolving cylinder, *A*, and the inside of the cup, *B;* 10 cubic centimeters in the cup, *C;* and 5 cubic centimeters in the test tube, *S*. The remaining 15 cubic centimeters are distributed throughout the tubing in the rest of the circuit.

In the experiments reported here the circuit was always filled with blood from another

cat prior to the experiment. The blood was obtained under sterile precautions from a donor cat, usually the day before, and an equal volume of salt solution was given the donor animal to replace the blood loss. Large cats, 3 or 4 kilograms in weight, were used as blood donors, and a blood loss of 65 or 70 cubic centimeters, representing approximately a fifth of their total blood volume, was withstood with very little disturbance. The animal was given 10 milligrams of heparin per kilogram of body weight prior to the withdrawal of the blood. The heparin used was obtained from the University of Toronto, and contained 15 units per milligram. The blood which was obtained was kept in a sterile flask in an icebox until the following morning when it was used.

The pumps are capable of delivering approximately 500 cubic centimeters of fluid per minute. As has been mentioned, the flow through the extracorporeal circuit is regulated by varying the speed of the pump, *F*. As the pump, *F'*, follows passively the variations in output of the pump, *F*, the rate of flow of blood through the entire extracorporeal circuit can be regulated by the rheostat controlling the speed of the motor, *G*. By collecting and measuring the volume of fluid delivered by the pump, *F*, at different rates of revolution of the pump, the volume delivered by one revolution of the pump was found to be constant at all rates of revolution. It was consequently a simple matter to calibrate the rheostat so that flow of blood through the circuit at any moment can be accurately determined from the position of the rheostat.

METHOD

The cat was used in these experiments because its oxygen requirement is small, and the oxygenator which had been built did not introduce enough oxygen into venous blood to maintain life in a larger animal. In all the experiments reported in this paper the blood flow through the heart and lungs was completely stopped for varying lengths of time by clamping the pulmonary artery. During the period in which the pulmonary artery was occluded, life was maintained by continuously withdrawing blood from the superior vena cava, oxygenating this blood, and injecting the oxygenated blood into the aorta by way of the carotid artery. Thus the extracorporeal circuit temporarily performed the functions of the animal's heart and lungs.

In the cat the lungs completely overlie the pericardium, and in order to expose the pulmonary artery artificial respiration must be employed, because the left pleural cavity has to be opened. This was an undesirable feature in these experiments, as it precluded the observation of natural respiratory movements when the pulmonary artery was occluded. To obviate this difficulty, a preliminary operation was performed 6 weeks before the cats were to be used in the perfusion experiments. This preliminary operation consisted of suturing the pericardium directly beneath the skin so that later the pulmonary artery could be rapidly exposed without opening the pleural cavity. Artificial respiration and anesthesia were maintained by the intermittent insufflation of air and ether vapor through a catheter inserted in the trachea through the mouth. A portion of the pectoralis major and minor muscles overlying the fourth and fifth costal cartilages was removed, and these cartilages together with bits of the adjacent ribs were resected. The left pleural cavity was opened through the bed of the fifth costal cartilage and rib. The portion of the pericardium overlying the pulmonary artery was then sutured to the margins of the opening in the chest wall with interrupted sutures of fine silk, and the skin incision was closed. This procedure made it possible some 6 weeks later to expose the pulmonary artery in a normally breathing animal by merely incising the skin and the underlying pericardium.

For the perfusion experiments the cats were anesthetized with ether. A catheter was inserted in the trachea through the mouth, and connected with a closed circuit containing 2 Krogh respiratory valves, a soda-lime chamber, a distensible rubber bag, a spirometer containing oxygen, and an ether vapor bottle. The use of this carbon dioxide absorption technique permitted a more easily controlled anesthesia than did the simpler open-drop ether method, and ensured the avoidance of anoxemia throughout the period of anesthesia.

The skin and parietal pericardium overlying the pulmonary artery were incised. The pulmonary artery was dissected free from the aorta and a graduated clamp (11) with its jaws open was put in place about the pulmonary artery. A small incision was then made on the right side of the neck and the right external jugular vein and the right common carotid artery were isolated. Ten milligrams, or 150 units, of heparin per kilogram of body weight, dissolved in sterile saline, was injected into the jugular vein. The artery was then ligated and a glass cannula was inserted caudad to the ligature pointing toward the aorta and tied in place. The cannula and tubing were previously filled with saline to avoid the introduction of air into the circulation. Similarly the external jugular vein was ligated and a venous cannula of stainless steel was passed through the external jugular vein down to the superior vena cava.

The venous cannulas used were made of stainless steel tubing with a very thin wall and an internal diameter of approximately 1.5 millimeter. The cannulas had 2 slight curves to correspond to the shape of the external jugular and innominate veins. They were 7 centimeters long. When tied in place, the tip of the cannula lay in the superior vena cava just beyond the junction of the innominate veins. To obtain the proper curvature of these venous cannulas, a Wood's metal mold of these veins had been made in a cat of average weight. The curves allowed the cannula to lie without tension in a position conforming to the normal course of the veins. This was of some importance because it was necessary to have the open tip of the cannula pointing caudally in the approximate center of the upper portion of the superior vena cava. If the tip of the cannula lay against or close to the wall of the vena cava, the vein wall was drawn into the tip of the cannula when very slight degrees of suction were exerted. The cannula had to be long enough to extend into the superior vena cava, as it was found to be extremely difficult to obtain an adequate flow of blood through the cannula when the tip lay in the jugular or innominate veins.

Before the operative work on the animal was begun, the extracorporeal circuit was thoroughly rinsed by pumping 2 liters of physiological saline through the apparatus. A 1:1000 aqueous solution of metaphen was then circulated through the apparatus for 20 minutes. The metaphen was washed out of the circuit with 2 liters of sterile physiological saline. Blood from the donor cat was then introduced and pumped slowly, at 100 cubic centimeters per minute, through the circuit until the temperature of the blood reached 38.5 degrees C. Shortly before the circuit was to be connected with the animal, a flow of 95 per cent oxygen and 5 per cent carbon dioxide was started through the oxygenator at the rate of 5 liters per minute. Faster rates of flow did not prove more effective in oxygenating venous blood. When the blood had reached the proper temperature and the operative procedures had been completed, the stopcock, *R*, was turned connecting the artificial circuit with the animal's vascular system.

After the extracorporeal circuit was connected with the animal and the donor blood had thus been mixed with that of the experimental cat, the pulmonary artery was gradually occluded by the clamp. During this time the rate of flow of blood through the extracorporeal circuit was gradually increased so that when the pulmonary artery was completely occluded the rate of flow of blood through the apparatus was approximately 100 cubic centimeters per minute per kilogram of body weight. Smaller rates of flow were generally found to be insufficient to maintain an adequate blood pressure, and it was difficult to obtain rates of flow appreciably higher than this.

In order to maintain anesthesia while the pulmonary artery was completely occluded, it was necessary to pass ether vapor through the oxygenator. The use of barbiturates intravenously or intraperitoneally would have obviated this necessity, but these anesthetics generally tended to depress the blood pressure and recovery from them was always unduly prolonged. Ether did not depress blood pressure and recovery from the anesthetic was rapid. The transference from ether vapor in the lungs to ether vapor in the oxygenator was made at the start of the compression of the

pulmonary artery by shutting off the supply of ether to the closed respiratory circuit and introducing ether vapor to the stream of oxygen going to the oxygenator. With care an adequate depth of surgical anesthesia could be maintained during the transference of ether vapor to the oxygenator and during the period of complete occlusion of the pulmonary artery. When the pulmonary artery was released, the procedure was reversed, i.e., ether vapor was again introduced into the closed respiratory circuit connected with the intratracheal catheter and was shut off from the stream of oxygen entering the oxygenator. It was necessary to maintain an even level of anesthesia, as any movements on the part of the animal were apt to produce occlusion of the tip of the venous cannula and cessation of blood flow through the circuit. With experience a skilled anesthetist could maintain an adequate, even level of anesthesia throughout the procedure.

The complete occlusion of the pulmonary artery was maintained for periods of from 10 to 25 minutes, inclusive, in the experiments here reported. At the end of this interval, the clamp was removed from the pulmonary artery. The flow of blood through the extracorporeal circuit was gradually decreased and, after a few minutes, was stopped completely, at which time the animal's heart and lungs again took over their normal functions. At this time a sample of blood was withdrawn for a hematocrit determination. The cannulas were removed from the carotid artery and external jugular vein, these vessels were ligated and the skin sutured. The wound in the chest was closed by approximating the parietal pericardium with several interrupted silk sutures, and the skin was closed without drainage. The postoperative convalescence of these animals was not remarkable. In several instances 100 cubic centimeters of 5 per cent glucose in physiological saline were given intraperitoneally for a day or so after operation.

RESULTS

Thirty-four experiments were performed under non-sterile conditions to test the new apparatus and to study survival of animals up to 8 hours. In these experiments the pulmonary artery was completely occluded, usually for 30 minutes, while the extracorporeal circuit maintained life in the animal's tissues. At the end of this time, the clamp was removed from the pulmonary artery, the cannulas were removed from the neck, and the wounds were sutured. The animals were then observed and if alive at the end of 6 or 8 hours, were sacrificed. Kymograph records were made of the blood pressure and respiration during the occlusion of the pulmonary artery while life was maintained by the extracorporeal circuit. In the course of these acute experiments many technical difficulties were solved, and it was demonstrated that the new apparatus was more efficient than the one previously described (9).

In 39 cats the pulmonary artery was completely occluded and life maintained by the extracorporeal circulation with complete aseptic precautions. In 13 instances with periods of occlusion of the pulmonary artery of from 10 to 25 minutes inclusive, the animals survived 24 hours or more. Table I gives the details of these 13 experiments. An average of 10 minutes was taken to compress the pulmonary artery. The time was somewhat shortened in the later experiments. It would, of course, have been possible to occlude the pulmonary artery suddenly, and to start the flow of blood through the artificial circuit abruptly. However, such a procedure would have resulted in a temporary fluctuation in blood flow and blood pressure and some disturbance in the level of anesthesia. It was found more satisfactory to occlude the pulmonary artery slowly and while doing so to increase the flow of blood gradually through the extracorporeal circuit. This gradual occlusion allowed the anesthetist to maintain an even depth of anesthesia during the transference of ether vapor from the animal's lungs to the oxygenator.

The periods of complete occlusion of the pulmonary artery were not long because of the difficulty in supplying an adequate amount of oxygen. The blood which returned to the animal's aorta was frequently not bright red. Hence it is probable that throughout the period of occlusion of the pulmonary artery there was always some degree of anoxemia and anoxia of the animal's tissues. This difficulty

was due to the fact that the surface for filming of blood in the oxygenator, 2300 square centimeters, was not large enough for the rates of blood flow used. An oxygenator with a 75 per cent increase in filming surface is being constructed at present, and it is hoped that it will correct this difficulty.

After the clamp was removed from the pulmonary artery the flow of blood through the extracorporeal circuit was continued at a gradually diminishing rate for an average period of 11 minutes. The object of so doing was to relieve the right ventricle, which was always somewhat distended during the period of occlusion, of the sudden burden of reassuming immediately its entire function. The necessity, however, for such a period of partial aid to the heart following the occlusion of the pulmonary artery has not been conclusively demonstrated.

The average rate of blood flow through the extracorporeal circuit during complete occlusion of the pulmonary artery was 242 cubic centimeters per minute, while the rate per kilogram of body weight averaged 99 cubic centimeters per minute. Rates of flow below 100 cubic centimeters per kilogram of body weight per minute were generally inadequate to maintain normal blood pressure. The relationship between the blood pressure and the flow of blood per kilogram of body weight through the extracorporeal circuit was borne out by observations in 14 non-sterile experiments. In these experiments the blood pressure was recorded directly from the femoral artery by a mercury manometer. Forty-six simultaneous readings were made of the systemic arterial blood pressure and the flow of blood through the extracorporeal circuit. When these points were plotted there appeared roughly to be a direct relationship between the flow through the circuit and the blood pressure, although, to be sure, many other factors are involved in the maintenance of the blood pressure. Consequently, an attempt was made in all experiments to maintain a flow through the extracorporeal circuit of 100 cubic centimeters per kilogram of body weight or more per minute.

The blood pressure was not recorded in the sterile experiments. Direct blood pressure readings would have required a third operative wound and the ligation of another peripheral artery at the end of the experiment, in addition to the necessity of maintaining sterility of the fluid in the circuit leading to the mercury manometer. Some time was spent in attempting to obtain satisfactory, indirect blood pressure readings by the use of pneumatic cuffs on the animal's hind limbs. Good correlation was obtained between this indirect method and direct readings with large ranges of blood pressure in the normal cat. However, the method failed to produce satisfactory readings during complete occlusion of the pulmonary artery. This was probably due to a combination of intense vasoconstriction and an insufficient pulse pressure. The 2 cuff method used was dependent upon a large pulse pressure for accurate readings.

There was usually some anemia at the conclusion of the experiments. In the 13 observations recorded in Table I the hematocrit readings at the end of the experiment varied between 25 and 40 per cent with an average value of 32 per cent. Hematocrit readings were also made after the operative work had been completed and before the animal had been connected with the extracorporeal circuit in 25 experiments. These readings varied between 25 and 44 per cent with an average value of 36.4 per cent. Hence for the most part anemia was present prior to beginning the perfusion.

In discussing the length of time these animals survived the experiments, it is convenient to divide them into 3 groups. The first group consists of 5 cats that survived from 24 to 48 hours, (experiments Nos. 9, 30, 31, 37 and 39). The chief factor in the death of these animals was undoubtedly anoxemia during the period of occlusion of the pulmonary artery due to inadequate oxygenation of the blood in its passage through the circuit. Lowered blood pressure, shock, and fatal lowering of the body temperature were contributory factors. The second group consists of 4 cats that lived a week or more (experiments Nos. 13, 15, 27, and 28). No. 15 was sacrificed on the eighth day because of purulent pericarditis. Pericarditis developed in No. 28, and was drained on the thirteenth postoperative day. Despite this the cat died 2 days later. No. 27 died on

the twenty-second day from a severe case of distemper. No. 13 died on the twenty-third day after having developed very intense jaundice. Extensive hepatic necrosis was found at autopsy. The third group consists of 4 cats that survived more than a month in a healthy condition (experiments Nos. 16, 20, 34, and 38). No. 20 was alive and perfectly well 34 days after a 20 minute period of complete occlusion, but was unfortunately sacrificed at that time by another investigator through a mistake in identification. The 3 remaining animals are alive and well, 12, 9, and 9 months, respectively after the experiment. These cats appear normal in every respect and show no neurological changes or abnormalities in behavior. One of these, No. 16, has had a litter of kittens since the experiment.

A number of control experiments have been performed in which the pulmonary artery was occluded under identical circumstances with the exception that the extracorporeal circulation was not employed. In these controls, which will be reported in detail elsewhere, regular respirations ceased within 40 seconds of complete occlusion of the pulmonary artery. There was an occasional solitary gasping respiration after the cessation of regular respiratory movements. Such isolated respiratory gasps were never observed after 3 minutes of complete occlusion. The blood pressure fell rapidly to zero within 30 seconds, and remained at this level throughout the period of occlusion. Coincident with the fall in blood pressure the retinal arteries contracted and could be seen only as thin lines. There was a slow movement in the retinal veins associated with a beaded appearance which persisted for a minute or so. This movement in the retinal veins also ceased completely after 3 minutes of occlusion. Under the conditions of the observations, if the clamp was removed from the pulmonary artery after 3 minutes of occlusion a spontaneous restoration of the blood pressure and resumption of respirations occurred. With longer periods of occlusion it was necessary to employ artificial means in order to restore cardiac and respiratory action. The means used were the intra-arterial injection of adrenalin and coramine in a central direction, washed in with 10 or 15 cubic centimeters of salt solution, and, when necessary, artificial respiration and cardiac massage. These were found to be the most effective methods of resuscitation. Even with the employment of these measures it was found impossible to initiate either respiratory or cardiac action after a period of occlusion of the pulmonary artery of 10 minutes. Permanent neurological damage has been found to exist after periods of occlusion of 4 minutes, as will be reported later in detail. In the observations with the extracorporeal circulation reported here none of these methods of resuscitation were employed or were necessary. With the extracorporeal circuit the respirations were regular, although often slightly more rapid and of greater depth throughout the period of occlusion, and the heart continued to beat strongly and at a regular rate throughout.

CLINICAL POSSIBILITIES

As far as we are aware, this constitutes the first report of the successful temporary substitution of an entirely mechanical apparatus for the functions of the heart and lungs of an animal followed by the prolonged survival of the animal. It is hoped that the method may eventually be perfected to such an extent that it may be safely employed on human beings. The difficulties do not seem to be insurmountable with regard to such an application. Heparin now has been purified greatly and is without toxic effects when given intravenously to human beings. Murray and Best have already prolonged the coagulation time of the blood to two or three times its normal value in patients for a number of days. Knoll and Schurch have rendered the blood of donors incoagulable by the injection of heparin prior to withdrawing blood for transfusion. In these patients after fairly large doses of heparin the coagulation time of the blood returned to normal limits within 150 minutes. That it is possible to perform an operation on an animal whose blood has been rendered incoagulable by heparin has been demonstrated in the experiments here reported. Silk technique has been used throughout and careful attention to hemostasis has been employed. The wounds in the chest and the neck have been closed with-

TABLE I.—SUMMARY OF THIRTEEN EXPERIMENTS

Experiment Number	Weight of cat kg.	Time of occlusion of pulmonary artery		Time artificial circulation continued after release min.	Time required for experiment min.	Blood flow through circuit during complete occlusion		Hematocrit at end of experiment per cent	Time of survival days
		Partial min.	Complete min.			Rate—c.cm. per min.	Rate per kg. body weight—c.cm. per min.		
9	2.25	22	15	16	108	225	100	28	1
13	2.2	22	10	11	143	240	109	30	23
15	1.9	15	10	13	132	190	100	32	8
16	2.85	10	12	5	114	250	88	33	370+
20	3.2	11	20	18	117	270	84	32	34
27	2.6	12	10	9	92	198	76	40	22
28	3.3	6	12	14	107	280	85	34	15
30	2.3	7	15	14	98	235	102	36	2
31	2.2	6	15	12	96	280	127		1
34	2.55	8	13	11	89	255	100	34	293+
37	2.8	8	25	8	93	260	96	34	1½
38	2.1	5	18	7	97	234	111	25	279+
39	2.1	4	15	9	98	230	109	27	2
Averages	2.5	10.4		11.3	106	242	99	32	

+Animals still living.

out drainage and no hematomas have developed. The only infections encountered were 2 instances of purulent pericarditis (experiments Nos. 15 and 28), and it is difficult to attribute these to the use of heparin.

The possible uses of such an extracorporeal circulation in humans may be briefly noted. If it were not at first feasible to carry an entire circulation with an oxygen requirement of 200 cubic centimeters per minute or more, it might be valuable temporarily to take over a small part of the cardiorespiratory functions in an acutely failing heart from whatever cause, where the possibility exists that the heart and lungs may again be able to assume their full burden. In patients with massive pulmonary embolism, even without carrying the entire circulation, the extracorporeal circuit might make the difference between life and death until a pulmonary embolectomy could be done to remove the embolus. And finally, if the entire circulation could be carried temporarily by an extracorporeal circuit, it is conceivable that a diseased mitral valve might be exposed to surgical approach under direct vision and that the fields of cardiac and thoracic surgery might be broadened.

SUMMARY

1. A method has been described by which life can be maintained in animals when the flow of blood through the heart and lungs is completely stopped by clamping the pulmonary artery. The method consists of the continuous withdrawal of blood from a peripheral vein, the introduction of oxygen into the blood, and the continuous return of the oxygenated blood to the animal's arterial system through a peripheral artery.

2. The essential features of the apparatus are a pump to withdraw the venous blood, a revolving cylinder on the sides of which the blood is oxygenated, and another pump to inject the blood into the animal's artery.

3. The difference between this method and those used for the perfusion of isolated organs lies in the added technical difficulties entailed in the use of small peripheral vessels for the perfusion. The vessels must be of such small size that their ligation does not result in any impairment of nutrition or function of the tissues supplied by them. The use of such peripheral vessels permits the animal's heart and lungs to resume their normal functions again after removal of the clamp from the

pulmonary artery and the cessation of the extracorporeal circulation.

4. Thirteen experiments are reported in which this method was employed. In these experiments the pulmonary artery was completely occluded for from 10 to 25 minutes, during which time life was maintained by an extracorporeal circulation. Five animals lived 24 to 48 hours after the experiment. Four animals lived from 8 to 23 days after the experiment. Finally, 4 animals lived from 1 to 9 months after periods of occlusion of the pulmonary artery of from 12 to 20 minutes. These 4 animals were normal in every respect and exhibited no neurological changes.

5. Control experiments, performed under identical conditions with the exception that the extracorporeal circulation was not used, have demonstrated irreparable neurological changes with periods of occlusion of the pulmonary artery of 4 minutes or longer, and have also shown the impossibility of restoring life after a 10 minute period of occlusion of the pulmonary artery.

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THIRTY-THREE PREGNANCIES IN DIABETIC WOMEN

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THE association of diabetes and pregnancy is relatively infrequent, and there is a striking lack of agreement concerning the proper treatment of the diabetic woman who becomes pregnant. An additional series of patients, managed conservatively, is reported.

During the 12 year period, July 1, 1926, to June 30, 1938, 33 babies were born to 28 diabetic mothers among a total of 9,105 delivered women; an incidence of 1:276. This figure is three times greater than that reported by Kramer and by Potter and Adair and probably is biased because selected patients are received from a large geographic area. The majority of these patients were observed only during the last month of pregnancy, but in several instances it was possible to follow the individual throughout gestation. Their ages ranged from 17 to 43 years. There were 5 nulliparæ; each of the 23 remaining women having been pregnant at least once, and 11, six or more times.

The diabetes was considered "severe" when the daily insulin requirement was 25 or more units, and "mild" when it was less than 25. According to this criterion, the classification of the diabetes depended upon whether the woman was pregnant or had been delivered. Prior to delivery 21 women had "severe" and 12 "mild" diabetes. Postpartum, only 14 women could be classed as "severe" diabetics. Three women were observed in 2, and one woman in 3 pregnancies. Two of the 3 women required more insulin during the second than during the first pregnancy and puerperium. The insulin requirement of the 2 other women was extremely labile.

CLINICAL FEATURES

Antepartum. In general, the antepartum courses were not marked by untoward manifestations. Two patients suffered from diabetic coma before term; both were delivered of living children. One of these patients had severe diabetes mellitus associated with diabetes insipidus. This combination of pregnancy, diabetes mellitus and insipidus, represents the only recorded case of the kind. (Greene and Gibson) The baby succumbed from proved intracranial hemorrhage 48 hours after a low forceps delivery at term. Another patient, whose daily antepartum insulin dosage averaged 100 units, had numerous hypoglycemic reactions during pregnancy but was delivered of a living child. One patient developed gangrene of the third finger of the right hand following a traumatic fracture during the sixth lunar month of pregnancy. Amputation a few weeks later resulted in complete recovery, and a live baby was born at term. Another patient developed hydramnios —2000 cubic centimeters of amniotic fluid measured at delivery—but the baby, weighing 4,300 grams at birth, survived. Eight pregnancies were further complicated by nonconvulsive toxemia, an incidence of approximately 24 per cent, which is definitely higher than the incidence (8.6 per cent) for the entire obstetric service during 1937. This finding agrees with the recorded experiences of White, Herrick and Tillman, Potter and Adair, and Joslin. There was no case of eclampsia among the diabetic patients.

One patient suffered with severe antepartum pyelitis but was delivered of a living child. Another patient experienced a few days of mild fever because of an upper respiratory infection. There was no other febrile reaction observed during the antepartum period. There were several incidental complications, such as arthritis, varicosities, hernia, scabies, gonorrhea, and yeast vaginitis.

No abortion occurred in any patient during her period of observation. In order to realize a more representative picture of abortion the entire reproductive careers of the 28 women were analyzed. Before the diabetes was recog-

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nized, there were 84 pregnancies, resulting in 15 abortions (17.9 per cent), 10 term and premature stillbirths (11.9 per cent), and 59 surviving children (70.2 per cent); whereas after the known appearance of the disease there were 39 pregnancies, with 11 abortions (28.2 per cent), 16 stillbirths (41.0 per cent), and 12 surviving children (30.8 per cent). The probable explanation for the comparative absence of antepartum complications, such as acidosis and coma, hypoglycemic shock, fever, and abortion, reported by many authors (1, 3, 4, 5, 6, 11, 12, 13) lies in the fact that most of the patients first came under observation late in pregnancy.

Labor. There were 28 spontaneous deliveries, 2 breech extractions, 2 outlet forceps operations, and 1 cesarean section. All operative deliveries were performed because of obstetric indications.

Postpartum. There was no maternal death. In 5 patients, or 15.3 per cent, the postpartum temperature rose to 100.4 degrees F. or above, but in only 1 instance, or 3 per cent, a low forceps delivery, did the fever persist for more than 24 hours.

The observations on this series of patients add relatively little toward solution of the old problem concerning the functional activity of the fetal pancreas in maternal diabetes. The postpartum maternal insulin requirement remained identical or was decreased in 24 and increased in only 9 patients. Of these 9 women, none fed her baby wholly by breast. Two, or 22 per cent, fed them by a combination of breast and formula, whereas 7, or 78 per cent, did not lactate beyond the first few puerperal days. Of the 24 women with identical or decreased puerperal insulin requirement, 15, or 63 per cent, fed their babies wholly or partially by breast, whereas 9, or 37 per cent, did not lactate beyond the first few days. These figures do little more than suggest that the elimination of sugar in the breast milk may serve to decrease the maternal puerperal insulin requirement. Although certain authors (1, 4, 5, 13) state that lactation in the diabetic woman is inadequate, 17 of the 27 surviving babies were wholly or partially breast fed.

Babies. Twenty-seven, or 81.8 per cent, of the babies survived. Four of the 6, non-surviving babies were stillborn and 3 were macerated. The non-macerated stillborn baby weighed 1,750 grams. The birth weights of the three macerated babies were 4,845, 3,915, and 2,675 grams. One baby, weighing 2,510 grams, died 24 hours after birth, presumably from hypoglycemia although no blood sugar determination is recorded. No autopsy was permitted. The sixth fatality involved a 3,850 gram baby who died 48 hours after a low forceps operation terminating a labor lasting 2 hours and 50 minutes. Sufficient intracranial hemorrhage to cause death was revealed at autopsy. Hypoglycemia was suspected in only 2 of the surviving babies; 3 hours after birth the blood sugar of 1 was 27 milligrams per cent. Fifty cubic centimeters of 5 per cent dextrose solution were injected subcutaneously with prompt relief. The other child was given glucose intramuscularly on the delivery table, did not nurse well for the first few days and 3 days after delivery was found to have a blood sugar of 30 milligrams per cent. Following further administration of glucose it recovered. The comparative absence of hypoglycemic reactions in the newborn child is probably explained by the fact that blood sugar estimations were not done routinely. Hypoglycemia is admittedly a potent danger in children of diabetic mothers, and recognition of its appearance is essential.

The birth weights of the 34 babies averaged 3,551 grams, and ranged from 1,750 to 4,845 grams. Labor was induced in only 11 cases. There were no congenital anomalies; none of the surviving babies was febrile, and all of them appeared to have normal vitality.

INDICATIONS FOR OBSTETRIC OPERATIONS

These patients were managed conservatively and concern was directed toward the diabetes rather than toward the pregnancy. A controlled diabetic who becomes pregnant is, obstetrically speaking, a normal woman. With this principle as a guide, none of the patients was subjected to induction of labor or to operative intervention merely because she was diabetic. The usual rules of conservative obstetrics were followed and interference was instituted only for obstetric reasons, accepted in the non-diabetic.

The choice of the method of delivery has received much comment from many authors and cesarean section prior to term is enjoying increasing favor (5, 10, 11, 13). When done on the diabetic pregnant woman the indication must be viewed as *fetal* and not as maternal. Generally speaking, the advocates of abdominal delivery are in agreement with this view. Priscilla White is especially emphatic in her belief that cesarean section is indicated, and says, "Prevention of the death and decay of the over-ripe fetus of the diabetic mother is a challenge today to the obstetrician and research worker in the field of diabetes. . . . Premature delivery of the fully developed though chronologically premature infant of the diabetic mother by cesarean section is the obstetrician's successful answer to the challenge." In her series of 66 personally observed patients, there was a fetal salvage of 89.0 per cent, which may be compared with the fetal survival rate, 81.8 per cent, of the present series of patients under conservative management. Assuming, for the sake of argument, the 4 stillborn babies in this series might have been saved by abdominal delivery, although one of them weighed but 1,750 grams, 32 otherwise unindicated cesarean sections would have been necessary. This seems a prohibitive price to pay for 4 babies, especially after Plass (7, 8) and others have repeatedly called attention to the fact that cesarean section does not in itself conserve fetal life. On the contrary, the fetal mortality rate from cesarean section alone ranges between 8 and 16 per cent.

CONCLUSIONS

Thirty-three pregnancies occurring among 28 diabetic women have been observed during a 12 year period. The incidence of pregnancy and diabetes was 1:276 obstetric patients.

Obstetric operations were done only when indicated and not because of the diabetes. There were no maternal deaths and only one woman developed a fever which persisted more than 24 hours.

Twenty-seven, or 81.8 per cent, of the babies survived.

Although the series is numerically small, the figures demonstrate that good results can be obtained by the conservative management of the pregnant, diabetic woman.

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CONGENITAL BOWING AND PSEUDARTHROSIS OF THE LOWER LEG

Manifestations of von Recklinghausen's Neurofibromatosis

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PSEUDARTHROSIS following fracture or osteoclasis during childhood in congenital bowing of the lower leg has been observed frequently (3). Scoliosis (1, 8, 10, 11) and excessive growth in length of long bones (5, 6, 7, 9) have received particular attention although no mention of them has been made in standard texts on orthopedic surgery or scoliosis. The association of pseudarthrosis and congenital bowing of the lower leg with von Recklinghausen's neurofibromatosis, which forms the theme of this article, seems thus far to have escaped notice in the literature of this country as well as that of Great Britain.

CASE HISTORIES

CASE 1. In February 1930, M.G., an Italian girl aged 2 months, was brought to the Charity Hospital Dispensary because of a deformity, present since birth, of her right lower leg (Fig. 1). The leg was acutely bowed anterolaterally, angle opened backward, in its lower third. In addition to the bowing there was considerable internal torsion. There was no history of trauma during or following birth and, except for a number of small areas of dark brown pigmentation scattered over her body (Fig. 2), she appeared quite normal. These areas of pigmentation were of interest because the mother (Figs. 3 and 4), who accompanied the child, was literally covered with neurofibroma molluscum. The mother expressed indifference to these brown spots on the child because she said that each of her 5 sons and one of her surviving daughters showed more spots than the patient and had never suffered any ill thereby. One daughter, aged 11 years, was free from these spots. In this family there had been 3 other children, prematurely born, whose sex had not been noted.

CASE 2. A brother, T.G., had sustained a fracture of his left lower tibia and fibula in June, 1927, when he was 15 years old. This went untreated for 8 days and was then cared for by the family physician for 10 months, during which period 5 operations were performed in attempts to get the bones to heal. On March 21, 1928, this brother was seen in the fracture clinic and referred to the orthopedic service. His left lower leg was somewhat swollen, red, and presented two discharging sinuses. There was nonunion of the bones of the lower third of his leg. Flexion contracture of 80 to 90 degrees was present in the left knee. Roentgenograms, since destroyed, showed two small sequestra. On March 24, 1928, sequestrectomy and curettage were performed. Healing of the bones and operative wound was not complete until June 29, 1929. Good function without symptoms continues to the present time.

A notation on the house record of this boy calls attention to a deformity, present since birth, of the left side of his chest, and also to a flabby, dull, brownish-colored tumor present in the usual position of the left nipple. The significance of these facts is now evident.

M.G. (Case 1) had been brought to the clinic to have the deformity of her leg corrected. Her family felt that some sort of operation should be done. Operative intervention seemed inadvisable for the following reasons: There was at that time under our care a child (M.M.) on whom several unsuccessful operative attempts, the last one by myself, had been made to obtain union in the lower tibia and fibula on which osteotomy for correction of anterior bow leg had been performed in 1922. Two other instances of pseudarthrosis of the lower leg following osteotomy in non-rachitic children remained vivid in my memory. A review of the literature at the time offered no helpful suggestion on the course of treatment to be followed. Consequently, M.G.'s family was persuaded to see what improvement might be obtained by daily manipulation.

On June 23, 1930, the patient was beginning to walk. When seen again on September 6, 1930, a tracing of the deformity compared with one made 5 months previously showed some improvement in the degree of curvature. Roentgenograms made on September 8, 1930 (Fig. 5), show the extent of the deformity then present. On October 22, 1931, the patient was walking well; the deformity was unchanged. She was not seen again until August 2, 1932, when the family was advised that operation for correction of the existing deformity should not be attempted until after adolescence.

The tendering of this advice was the consequence of hearing a paper on June 17, 1932,

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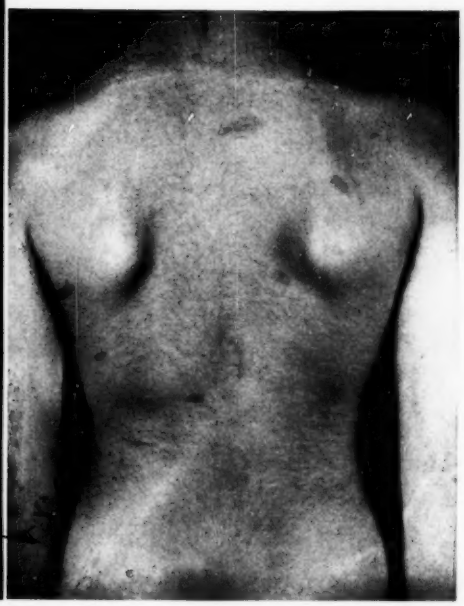

Fig. 1, left. Photograph of M. G. showing present lower leg deformity.
Fig. 2. Photograph of M.G. showing pigmented skin areas associated with von Recklinghausen's disease.

by Dr. Wallace Cole, at the meeting of the American Orthopedic Association, in Toronto, entitled "Congenital Non-union of the Tibia." Cole pointed out that even though bony union may occur early and seem quite firm and adequate physically as well as roentgenographically for a considerable period of time following osteotomy or fracture during childhood in congenital bowing of the lower leg, pseudarthrosis may later develop for no apparent reason. After adolescence operative correction was more successful for deformity and non-union (2).

Figures 6 and 7 show the degree of deformity recorded by roentgenograms made on February 6, 1934, and Figure 8 shows the condition on July 5, 1938. Figures 1, 2, and 8 illustrate the deformity and the associated pigmented skin areas as they now appear. In addition to the bowing the right leg is approximately ½ inch shorter than the left. No apparent functional handicap exists, and although the end-result here obtained fails to meet orthopedic ideals, it far surpasses the end-results obtained in the 3 cases which follow:

CASE 3. M.M., an Italian girl, was admitted to the orthopedic department on November 16, 1922, when she was 2 years old, because of a deformity, present since birth, of her left lower leg. Her father,

Figs. 3 and 4. Photographs of front and back of M.G.'s mother. Degree and extent of neurofibroma molluscum have not changed since M.G. was first seen in 1930.

Fig. 5.

Fig. 6.

Fig. 7.

Fig. 8.

Fig. 5. Roentgenogram of M.G. to show condition of deformity as it appeared on September 8, 1930, at the age of 9 months.

Figs. 6 and 7. Roentgenograms of M.G. to show condition of deformity of both legs on February 6, 1934, at the age of 3 years 2 months.

Fig. 8. Roentgenogram of M.G. to show condition of deformity on July 5, 1938, at the age of 8 years 7 months.

mother and 6 siblings were living and well. The patient had been breast fed for 15 months, began walking at 20 months, and, except for an occasional cold and some stomach trouble, had been well.

Examination showed a marked anterolateral bowing of the left leg in its lower third. Physical examination and roentgenograms of knees and wrists showed no evidence of rickets.

On November 17, 1922, osteotomy of the left tibia and fibula at the site of the deformity was performed and a plaster cast applied. Postoperative roentgenograms showed the deformity to be well corrected with the fragments in good position and alinement. On January 2, 1923, the plaster cast was removed, the operative wound was well healed, bony union was quite firm, and the deformity had apparently been corrected. A short walking plaster was therefore applied. Three weeks later the foot and lower leg were in good position, bony union was firm, and the deformity remained corrected. Massage to the foot and lower leg was prescribed twice daily and the patient began walking in 2 weeks.

On July 7, 1923, when she was next seen, the deformity had begun to recur and a brace was applied. By February 5, 1924, the deformity had recurred and she was admitted to the hospital for operation. The ends of the bones were freshened and a new plaster cast applied. On May 21, 1924, she was readmitted to the hospital because the deformity had increased. The following day resection of ununited fracture of the left lower leg was performed. Fibrous tissue was removed and the laterally overriding fragments of bone ends chiseled away. Fair approximation of the ends was obtained. On June 2, 1924, the patient was discharged from the hospital wearing a plaster cast.

In spite of physical and roentgenological evidence of favorable progress for a time and the continuous application of supportive apparatus for 3 years and 2 months, pseudarthrosis with deformity again developed. On July 18, 1927, open reduction of the left tibia was performed. The ends of the tibia were removed and the stumps tied in apposition with chromic catgut passed through drill holes. On August 11, the wound was clean and entirely healed. On September 27, the patient began to walk with the cast still on the leg. On December 10, the cast was removed. There was still some motion of the fragments though the position was good. A new cast was applied. On May 19, 1928, a brace was applied. On August 10, 1929, the patient was walking with a short brace. There was non-union in the lower third of her leg. The distal fragment was pointing laterally and posteriorly. On September 22, 1930, the following x-ray report was made: Left tibia and fibula show old ununited fracture of tibia about 3 inches above the ankle with fragments in apposition but with marked outward and posterior angulation. There was spiral bowing of fibula at the same level with no evidence of fracture.

On August 27, 1931, a massive bone onlay graft, the last operative attempt to obtain bony union, was performed. The area of pseudarthrosis was exposed and just enough of the bone ends resected to permit correction of the deformity. Two full thickness grafts obtained from the right tibia were placed in longitudinal grooves extending well beyond the fracture line of both tibial fragments. The grafts placed on opposite sides of the tibia were secured by 4 chromic catgut ties encircling them and the bone fragments. Bone chips obtained in making the grooves were placed alongside the grafts.

Fig. 9.

Fig. 10.

Fig. 11.

Fig. 9. Photograph showing deformity of M.M.'s leg with operative wounds. Scar over right tibia shows site where tibial graft was removed.

Fig. 10. Roentgenogram of both of M.M.'s legs. Right tibia and fibula show good mineralization. Note scars of interrupted growth in lower tibia. Left tibia shows osteoporosis with greater demineralization at lower ends which show the scars of interrupted growth, sclerotic bone surfaces at the site of osteotomy, and retarded growth in all dimensions.

Fig. 11. Photograph of M.M. showing café-au-lait spots characteristic of von Recklinghausen's disease.

On August 29, 1931, a roentgenogram showed that the grafts were holding the bones in good position and alinement. On September 19, a roentgenogram showed the graft and fragments in good position but there was still no callus. On September 30, a roentgenogram showed that the graft and fragments were still in good position and there was now apparent some evidence of callus. Reapplication of casts at regular intervals continued until March 29, 1932.

The patient did not report to the clinic as directed and was not seen again until August 23, at which time bony union was still lacking. She has been seen occasionally during the past 6 years. Figures 9 and 10 show the condition of her leg at the present time. The left leg now measures 27½ inches, the right, 30 inches. For the past 2½ years she has preferred to hobble about without any supporting appliance. Permission for further operative intervention has been refused.

Figure 11 shows the pigmented skin areas of chest and abdomen. These areas are present to a lesser degree in other parts of the body. The area beneath the left nipple is very deeply pigmented. The shadow at the umbilicus is intensified by brown pigmentation extending to its depths and somewhat irregularly beyond its borders.

The only other member of the family allowing examination was the father who has a number of small pigmented skin spots scattered irregularly over his body, a few of which are elevated from the surrounding surface; two of these spots are pedunculated. Several small round lumps can be felt in the skin but a diagnosis of von Recklinghausen's disease here would be presumptuous. The mother, likewise, presented suggestive evidence of the disease. She refused examination but there were a few brownish nodules visible on her face and neck and a patch of pigmented skin about 2 to 4 centimeters in diameter was plainly visible through the stocking on her right lower leg.

For the patient herself, now well beyond the age of puberty, there is hope of successful bony union provided fixation of the 2 ends of the tibia is permitted.

Case 4. A.T., (Figs. 12, 13, 14 and 15) a Hungarian girl, aged 14 years, was born with a crooked right leg. Her mother died from uterine hemorrhage following an interrupted 3 months pregnancy when A.T. was 3 years old. Three sisters are living and well. The father (Figs. 16 and 17), now 49 years of age, presents a typical picture of von Recklinghausen's neurofibromatosis, even to the frequently associated scoliosis.

A consultant recommended that A.T.'s leg be straightened by an operation but that this should not be done until she was 3 or 4 months old. Osteotoclasis of the right lower leg was performed, therefore, at the age of 4 months, but both tibia and fibula failed to unite. The hospital record states that on admission the degree of atrophy and deformity indicated amputation. On January 24, 1927, the right lower leg was amputated.

Although a diagnosis of von Recklinghausen's disease was not stated in the hospital record, some of the skin lesions seen in the accompanying photographs were thus described: "On the anterior surface of the right shoulder is a raised red lesion about

Fig. 12. Photograph of A.T. Note pigmented skin areas on shoulder, abdomen, and thigh.

Figs. 13 and 14. Photographs of A.T. showing site of amputation, typical café-au-lait spots, and neurofibroma molluscum characteristic of von Recklinghausen's disease.

Fig. 12.

Figs. 13, above, and 14.

Fig. 15. Roentgenogram of lumbar vertebral column and pelvis of A.T. Note congenital anomalies of lower lumbar and sacral region and associated scoliosis.

the size of a half dollar present since birth. It is bright red, slightly spongy, and quite sharply defined. Two large pigmented nævi are seen on the right side of the abdomen and 3 or 4 small ones on the back. The left shoulder shows a small, pea-sized papule similar to that on the right shoulder. The abdomen shows many scattered dry pinhead-sized red papules." The skin lesions as they now appear, excepting color variations, are well illustrated in Figures 13 and 14. Figure 15 shows congenital anomalies in the lumbar spine and sacrum and some structural changes in bone and soft tissue.

CASE 5. H.L.[1] is a Bohemian girl now aged 8 years. Despite full term, normal delivery, and a birth weight of 7½ pounds, she presented a congenital deformity in the lower third of the right leg (Figs. 18, 19, 20 and 21). The mother, 2 sisters and 2 brothers are living and well. One brother, born with a pyloric stenosis for which a successful operation was performed during the second or third week of his life, died from osteomyelitis at 11½ months. Another child was born dead at 8½ months. The father is living but is somewhat disabled from a severe bronchitis.

There is no evidence of rickets in the patient's history. She began to walk at about the age of one year. At 18 months, a fall to the floor while walking caused an injury to her deformed leg. The doctor to whom she was taken at the time found nothing more than a sprain so he strapped the leg with adhe-

[1]Presented through the courtesy of Dr. T. A. Willis.

Fig. 16, left. Photograph of A.T.'s father. Neurofibroma molluscum and pigmented skin areas quite definite.

Fig. 17. Showing back of A.T.'s father with typical café-au-lait spots and neurofibroma molluscum. Note degree and extent of associated scoliosis frequently present in von Recklinghausen's neurofibromatosis.

sive plaster. For the following 3 or 4 months, during which time the father attempted to care for the leg by repeated adhesive strapping, there was a gradually increasing deformity accompanied by pain, swelling, and disability.

The child was then taken to Dr. T. A. Willis who found an ununited fracture at the site of the injury. A plaster cast was applied and, with renewals at regular intervals, was worn for 2½ years without benefit. On August 19, 1934, when the patient was 4 years old, a bone graft operation was performed. Casts and braces have been worn continuously since that date.

Figure 22 shows the roentgenographic appearance of her leg 2 days before operation and Figure 23, 3 days after operation. In Figure 24, a roentgenogram made 1 year and 4 months after operation, union of the tibia is still wanting although the fibula has united. An interval of 2 years and 6 days elapsed from the time this roentgenogram was made until the most recent one (Fig. 25) was obtained. This shows that firm bony union is now present in the tibia as well as in the fibula. Manual examination and also the ability of the leg to withstand the entire body weight are further proofs of bony union. Because of the marked angulation and the degree of sclerosis present in the tibia, however, supportive apparatus for weight bearing is being continued.

The association of congenital bow leg, pseudarthrosis, and von Recklinghausen's disease has heretofore escaped attention but in the cases just presented the association is unequivocal. In the 4 girls bowing of the lower leg was present at birth. Pseudarthrosis followed fracture in one, osteoclasis in another, and osteotomy in a third. In one girl, Case 1, fracture and operative intervention have thus far been avoided. In the single male, T.G., brother of M.G., Case 1, definite evidence of deformity prior to fracture is wanting.

In the one family, the mother (Figs. 3 and 4) and 7 of 8 surviving siblings present typical lesions of the disease. In another family, the father (Figs. 16 and 17) shows external lesions in addition to the frequently associated scoliosis.

The evidence thus far advanced, though quite definite, might rightly be questioned as being conclusive for the thesis here proposed. The addition of these 5 cases to the 1 atypical and 9 typical cases already reported by Robert Ducroquet should dispel any doubt. Thirteen of 15 cases disclose a definite and identical etiology which is convincing even for a rare disease. The following is a brief review of Ducroquet's cases:

Pen., 10 years. We have no information on the father. The mother recalls a birth injury having provoked fracture. The child shows all the signs of a definite fibrous pseudarthrosis. She is covered with pigmented spots—"café-au-lait." We have attended this child for 3 years. The bones of the limbs have developed though union has never occurred.

Ben., 14 years. The mother who refuses to be examined attributes the fracture, which did not unite, to obstetrical traumatism. The child has a

Fig. 18, left. H.L. at 7 years with brace.
Fig. 19. H. L. without brace.

Fig. 20, left. Front view of H.L. to show pigmented areas on trunk.
Fig. 21. Back view of H.L. to show pigmented areas. Scoliosis functional.

typical pseudarthrosis with fusion of fibula to tibia. He has been operated on 6 times, one operation being a perifemoral sympathectomy. He is covered with café-au-lait spots. He has never walked without support.

Cos., 65 years. Heredity unknown, but his father had the same affliction, a pseudarthrosis which dated from birth at which time he had a broken leg. Patient presents a typical pseudarthrosis. He was not operated upon. A diagnosis of typical von Recklinghausen's disease was made. Patient was covered

Fig. 22.

Fig. 23.

Fig. 22. Roentgenogram of H.L.'s right leg August 19, 1935, showing deformity and non-union of tibia.
Fig. 23. Roentgenogram August 24, 1935, of right leg after operation.

Fig. 24.

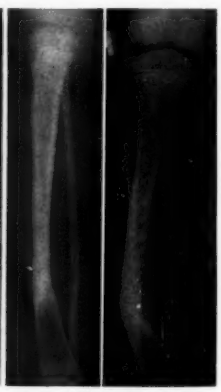

Fig. 25.

Fig. 24. Roentgenogram December 11, 1936, of right leg to show condition 16 months after operation.
Fig. 25. Roentgenogram December 17, 1938, of right leg to show present condition.

with pigmented areas and had cutaneous tumors, showing numerous neuromas.

Va., 4½ years. Mother who was covered with multiple spots refused to be photographed. Birth was normal. Mother thinks that a fracture originated then and never healed. There is typical tibia-fibula fusion. Patient's body is covered with pigmented spots.

Br., 3 years. No family history is given. He shows definite pigmented areas in the skin and malformation of the left tibia.

Bernard, 4½ years. Body is completely pigmented. The mother is 35½ years old. He presents a typical neurofibromatosis.

Mer., 12 years. The mother presents numerous spots. He has a congenital deformity of the tibia and multiple café-au-lait spots are noted. The mother thinks the deformation is increasing. At examination, the deformation showed an angle open behind. X-ray film shows posterior thickened area.

Tardi., 5 years. The mother presents certain café-au-lait spots. Definite deformation from birth has been present in both tibiæ, which has been growing worse. Osteotomy has been suggested. The two tibiæ are much curved inward and open behind; there is a polycystic condition in the area of deformation. X-ray films taken after 2 years show the condition slightly worse.

Thon., 37 years. There is present a congenital bowing of the leg with great shortening (20 centimeters). Delayed labor is noted in history. Isolated spots are present on the atrophied limb. X-ray films show shortening with a bowing of the tibia forward.

Cro., 2 years. Patient was born with a tibial deformity. Examination shows congenital pseudarthrosis in both bones of the leg, confirmed by the x-ray. The body of this infant is covered with spots which seem to be becoming darker.

Div. We cite, to recall it, the only case in which we have not been able to obtain any cutaneous evidence, pigmentary, or any growth associated with this congenital tibial lesion.

In these observations we see that among 7 patients a pseudarthrosis occurs in 5 and in 1 a congenital bending. One other patient showing congenital bending has a mother who suffers from von Recklinghausen's disease. Finally, in the last case of bending we find the marks both in the child and in the mother. Because of the same family history, it appeared logical to M. Ducroquet to combine these tibial deformities with pseudarthrosis.

A tibia which is congenitally deformed or bent or shows a pseudarthrosis may be a suspicious indication of von Recklinghausen's disease. This association has appeared so consistently that M. Ducroquet believes it possible that in the isolated instances where neurofibromatosis is not definitely mentioned, it would be possible, nevertheless, to find manifestations of von Recklinghausen's disease within the third or fourth generations.

The hereditary nature of von Recklinghausen's disease has been known for a long time but M. Ducroquet has verified it and brought new observations. There is one family in which the grandmother, the mother, and the daughter had all 3 signs, namely, bowed tibiæ, café-au-lait spots, and neurofibromatosis with accompanying scoliosis. In another instance the daughter showed isolated spots and scoliosis, and the mother presented the complete manifestations of cutaneous tumors, neuromas, and pigmentation.

SUMMARY AND CONCLUSIONS

Added to M. Ducroquet's cases are 5 cases in 4 of which definite bending of the lower leg is known to have been present at birth. In one case, that of M.G., fracture and operative intervention have been avoided and no functional handicap exists. In this case some improvement in the degree of angulation has taken place with growth. Osteotomy, osteoclasis, and fracture were each followed by pseudarthrosis in 3 cases. Pseudarthrosis followed fracture in the 1 case in which no history of bending could be obtained.

All of the cases here reported show typical lesions of von Recklinghausen's disease. In the one family in which congenital bowing occurred in one girl and pseudarthrosis following fracture in a brother, 7 of 8 surviving siblings show typical skin lesions and the mother is literally covered with neurofibroma molluscum.

In one child on whom osteoclasis was performed for the correction of bow leg, deformity and disability necessitating amputation followed. In addition to the typical skin lesions this child also presents congenital anomalies of her lumbar spine including a scoliosis. Her father shows the widely scattered skin lesions of von Recklinghausen's disease and the frequently associated scoliosis.

Roentgenograms of the long bones, skull, and pelvis show no cysts in either the children or parents so examined.

The association of pseudarthrosis with congenital bowing of the lower leg in childhood has been recognized and accepted by a few orthopedic surgeons, though published references of actual cases do not appear in the literature of this country.

The association of congenital bow leg, pseudarthrosis, and von Recklinghausen's neurofibromatosis has heretofore not been recognized, but that such an association does exist cannot be disputed on the findings of the cases here presented.

Associated cystic bone changes seldom accompany the condition. In only one case, that of Ducroquet's (Tardi.) there is in the area of deformation a polycystic condition.

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THE RÔLE OF FASCIA IN MYOSYNOVITIS AND ADHESIONS

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PATHOLOGICAL changes in the synovial covering of the fascial planes are a competent, producing cause of derangement of their normal gliding function in locomotion. The synovial covering of these planes is of mesodermal origin and is of clinical importance since the fascial surfaces are in intimate contact with the nerves and blood vessels as they traverse the fascial spaces. Involvement of this covering of the nerves in locomotion is believed to result in radicular muscular pain in certain patients.

The etiological diagnosis of muscular pain resulting from fascial pathology is strictly limited to patients in whom osseous pathology and other etiological factors have been excluded. Before conclusions can be drawn from the pathological slides comprising this preliminary report a rational understanding of the normal functional mechanics of the soft tissues in locomotion is necessary. Several reports of such a study have been made and will be reviewed briefly.

In 1935, determinations of the tensile strength of the fibrous tissues (5) which support the fascial planes were reported. In addition to the finding of normal tensile strength, changes in the tensile properties due to age, shearing stress, and also arthritis were studied. These findings were clinically correlated with the discovery that the fascial spaces function as joints for gliding motion between muscular planes (1). In the same year, fascial adhesions were demonstrated and photographed from cadaver studies.

In 1936, roentgenographic study of the fascial spaces were reported (2). Air was used as a contrast media and showed an even distribution in normal cases and irregularity was noted in arthritic patients. This is believed to be due to fascial pathology. By correlating the study with clinical work it has been possible to apply our findings to fascial surgery (3).

"Fascial planes function as joints synchronizing motion between muscles, groups of muscles, nerves, and blood vessels. Traumatic and inflammatory lesions may involve these planes, resulting in myosynovitis or fascial adhesions (4)."

These spaces actually enclose complicated gliding joints formed by the varying angles of contact of the fascial bundles and all are lined normally by a synovial layer of mesothelial cells corresponding in function to the synovia found in the joints between bones.

Such fascial joints are reinforced by fibers of the fascia and the complex arrangement permits function similar to that of the ligament and tendons surrounding the joints between bones. The synovial covering of the fascial spaces facilitates movement of the vessels and nerves in a manner similar to the movements of the viscera in the thoracic and peritoneal cavities.

The normal gliding function of these joints parallels the function of the tendon in its sheath. When traumatic or inflammatory lesions involve the tendon in its sheath, pain and limitation of motion result. A similar syndrome results if the function of fascial planes be retarded by like pathology with the addition of radicular muscular pain due to the nerves traversing these gliding joints.

Histologically these lesions are shown by altered secretions, focal thickenings of the opposing fascial surface mesothelium, or by actual adhesions.

The present brief report is limited to histopathology which in our opinion corroborates the concept given. The normal mesothelial layer covering the fascial surfaces is seen in

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Photomicrographs of certain of these slides were presented at a scientific exhibit of the 1938 session of the American Medical Association in San Francisco, California.

Presented before the American Society for the Study of Arthritis, New York Academy of Medicine, April 11, 1939.

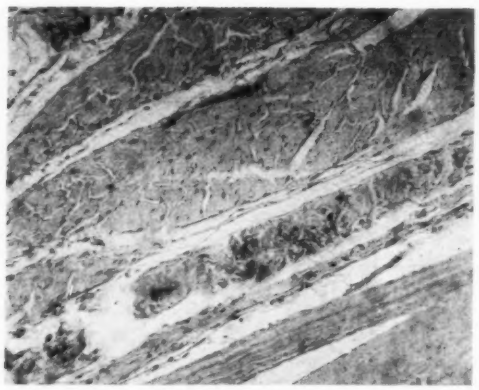

Fig. 1. Normal fascial covering—one layer of mesothelial cells.

Fig. 2. High power of mesothelial cells.

Figures 1 and 2 and in its simple form is a single layer of flattened cells.

It must be remembered that these tissues are of much smaller and more delicate arrangement than the synovial linings of larger cavities such as in osseous joints, the peritoneum and thorax. Hence, they are much more difficult to show histologically and their study must be closely correlated with their function. The origin of the cells lining these gliding joints is from the connective tissues as are other synovial membranes lining the joints referred to. The function of the synovial membrane in all these locations is to permit this gliding or rotatory motion between adjacent tissues.

Hyperplasia of the mesothelial cells lining the fascial joints (Figs. 3 and 4) may indicate a proliferative reinforcement in response to abnormal strain or to altered secretions from inflammation. This hyperplasia may interfere with normal nerve and blood vessel function without other clinical evidence of inflammatory reaction. With associated rheumatic

Fig. 3. Case 1, plantar fascia. Hyperplasia of fascial mesothelium (lower power) and myosynovitis.

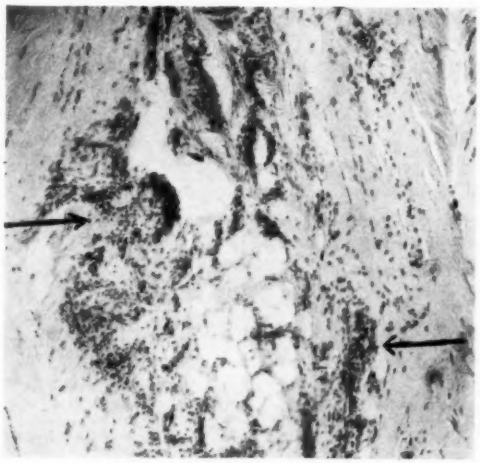

Fig. 4. High power of Figure 3. Note excrescences of mesothelium.

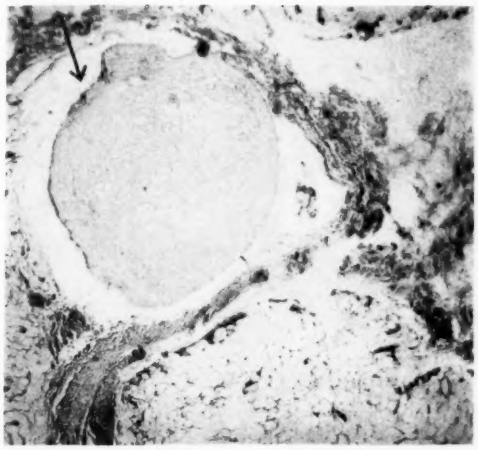

Fig. 5. Case 2, fascia lata. Mucoid degeneration of fascial fibers due to altered secretions.

conditions, the time of repair in this group of cases may be indefinitely delayed. This forms a part of the picture in hyperplasia of the ligamentum flava (7) and of the tensor fascia lata (8), interfering with normal nerve function of the lower back.

Case 1. W.G.F., male, aged 56. A pneumofasciagram was made on October 10, 1936, for the study of osteo-arthritic changes of the right foot. This showed adhesions involving the plantar fascia and a spur of the os calcis. Fascial adhesions were dissected free. The spur was removed and a fascial biopsy carried out on October 27, 1936. Fascial biopsy showed myosynovitis (Figs. 3 and 4). This patient has been symptom free and able to indulge in full activities up to the time of last examination, October 18, 1938.

Rupture of the fibers of the fascia by disturbing the normal continuity of the mesothelial surfaces is sufficient to cause altered secretions and disturbance of blood vessel and nerve function. Furthermore, these pathological changes are unavoidably linked up with impaired muscle function and the resulting changes in the lymphatic circulation.

Case 2. Male, aged 32. The patient suffered an infection from foreign body, a wooden splinter, in thigh. Biopsy specimen of fascia lata was obtained at the time of removal of the foreign body (Figs. 5 and 6).

Figure 7 from Case 3 shows fascial adhesions as they are seen in acute infective

Fig. 6. "Mucoid polyp" covered by mesothelium (high power of Fig. 5).

processes. This is probably the part the soft tissues play in the splinting of an acutely involved osseous joint.

Case 3. Male, aged 8, suffered from a septic arthritis of the hip. Fascia lata was removed by biopsy when the hip was drained. Temperature at time of operation was 104 degrees. Biopsy specimen through the courtesy of Dr. David Sloane. The patient was on the service of Dr. Lyman Weeks Crossman, City Hospital, New York City.

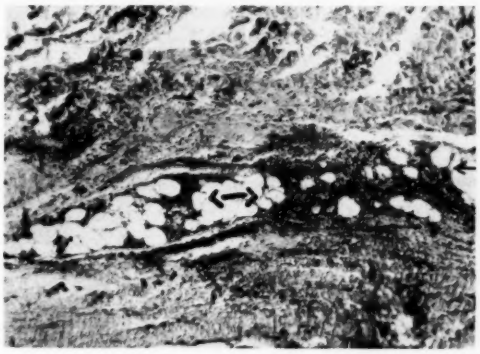

Fig. 7. Case 3, fascia lata. Four wide fascial adhesions cross the fat in the center of the field.

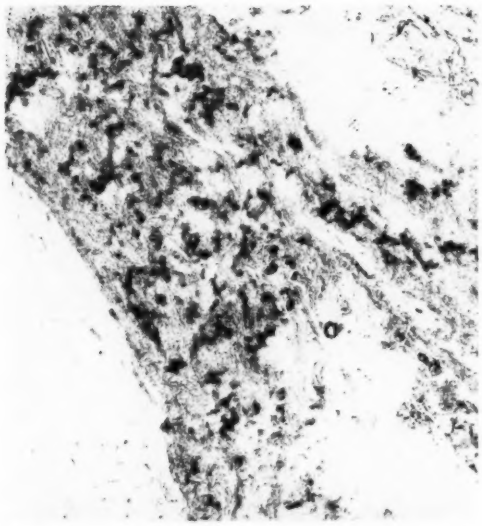

Fig. 8. Case 4, fascia lata. Calcific deposits scattered through the fascia.

In still other conditions—as lymphatic elephantiasis the abnormal strain on the fascia produces various types of degeneration as extravasations of lymph, deposits of blood crystals, and calcific deposits from ruptured capillaries and lymphatics.

Figure 8 from Case 4 shows calcific deposits scattered through fascia lata.

CASE 4. M. F. Female, aged 28, referred for surgical treatment by Dr. C. Whitney Banks, had a bilateral enlargement of thighs and both lower extremities of 14 years' duration. A clinical diagnosis of lymphangiectatic elephantiasis was made. Fascia lata biopsy specimen was obtained at the time of modified Kondoleon operation, October 17, 1938; incision from high on the left buttocks to beyond the left ankle. Living fascial sutures, left, attached at one end used to approximate partially the fascial surfaces before the skin was closed. Similar operative procedure on the right extremity and buttocks on October 27, 1938. Follow-up for over 10 months with a clinical and cosmetic result highly satisfactory to both the surgeon and the patient.

In cases of long continued trauma as in various occupations, actual bony plates are formed in the fascia as shown in Figure 9 from Case 5.

CASE 5. Male, aged 19, student, was a strenuous athlete, especially in baseball. He had a circumscribed area on the inner aspect of the thigh which had been present about a year. A clinical diagnosis of myositis interstitialis ossificans was made. (Reported through the courtesy of Dr. George Saypol.)

Fig. 9. Case 5, fascia lata. Bony plates in fascia.

As a result of the anatomical, roentgenographic, and biomechanical studies previously reported and confirmed by the histopathological studies mentioned, we believe that fascial pathology often reveals the true cause of radicular muscular pain. It would seem that many cases not previously diagnosed may well be designated myosynovitis or fascial adhesions. Moreover, there is reason to believe that the temporary success in some of these cases by massage and manipulation may be explained by the freeing of agglutinated fascial surfaces, the releasing of secretions, or by breaking adhesions, rather than by changing the anatomical position of osseous structures. The correlation of these studies tend to clarify the clinical management of patients suffering from pathological involvement of fascial planes.

In selected cases pneumofasciograms are used in an attempt to localize the pathology in addition to biomechanical measurements of the range of motion of the involved joints. These measures combined with very careful clinical study of the patients have been found of value in localizing the pathology. When operative procedures are indicated either on the fascial or osseous structures they are combined with the removal of biopsy specimens for pathological, and when possible, for biomechanical studies.

It is earnestly believed that further co-operative studies between these students of clinical surgery, pathology, and biomechanics will yield further facts concerning normal and pathological locomotion in man.

The authors desire to acknowledge their gratitude to Doctors Allen O. Whipple, Ward J. MacNeal, Charles Gilvy, Arthur Purdy Stout, George Hawley, S. N. Blackberg, and Arthur Steindler for their co-operation and Mr. K. L. Wegel of the Bell Laboratories and Prof. G. B. Karelitz of the School of Engineering, Columbia University.

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SULFANILAMIDE THERAPY IN SEVERE PUERPERAL INFECTION

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SULFANILAMIDE is widely used for the treatment of puerperal infection regardless of its etiology. Yet Colebrook and his co-workers (2, 3, 4), who have reported excellent clinical results, could find no satisfactory evidence that it was of any value in puerperal infections by organisms other than the Streptococcus hemolyticus. Approximately 15 per cent of Colebrook and Purdie's (4) cases showed hemolytic streptococci in the blood stream, and in more than half infection was limited to the uterus, vagina, and perineum. Many would have recovered without special treatment. Their experience with staphylococcus infections was limited, yet good enough to warrant its use. Clinical trial in genital tract infections by anerobic streptococci, non-hemolytic aerobic streptococci, viridans and coliform bacilli was inconclusive, though they had observed no convincing results. Pyelitis presents an entirely different problem. Successful treatment seems to depend upon concentration of sulfanilamide in the urine rather than the nature of the organism.

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For practical purposes the organisms causing severe forms of puerperal infection are few. That the streptococcus is by far the most important has long been known. It seems likely that streptococci in serological group A account for not more than about one-third of all cases of puerperal pyrexia, yet they cause 75 per cent of all the deaths, more than half occurring after spontaneous delivery. These infections are not endogenous, but originate from an extragenital source, usually the nasopharynx. Fry has never found these organisms in a vaginal swab before delivery, and believes that conditions in the normal genital tract are unfavorable for their survival. Dora Colebrook (5) has shown that hemolytic streptococci present in the vagina before labor, and the great majority of those present after delivery are relatively harmless, and, as a matter of fact, unable to initiate puerperal infection. At Queen Charlotte's group A is responsible for about 40 per cent of the severe cases, and about 75 per cent of the deaths due to infection. Anerobic streptococci are next in importance. Often both types A and B are present. Normally found in the vagina, and,

according to Hare, nowhere else, they thrive in the presence of severely traumatized tissue or necrotic secundines resulting from operative delivery, manual removal of the placenta and induced abortion. Anaerobic streptococci, rather than group A aerobes, should be suspected in cases of thrombophlebitis and bacteremia associated with these factors. Other organisms, with the exception of Bacillus coli in urinary tract infections, are relatively infrequent.

Since it is probable that sulfanilamide therapy is of little or no value in genital tract infections due to organisms other than Streptococcus hemolyticus group A, it is generally urged that differentiation of the organism should precede administration of the drug. That patients should be protected against unwise or unduly prolonged administration of a toxic drug is obvious. No doubt, prompt recognition of the etiology of the infection is important, yet bacteriological diagnosis can not always be made.

It is known that more than one organism may be responsible for the fever, and it is possible that the organism isolated may not be the etiological agent. To predicate treatment entirely upon bacteriological investigation may not be in the best interest of the patient. Though Bliss, Long, and Feinstone have shown that for practical purposes streptococci may be classified by cultural and biochemical methods alone, it is quite certain that for some time to come routine laboratories will not be equipped for accurate diagnosis of strains of streptococci. At any rate it is a fact that sulfanilamide is being widely used without any bacteriological investigation whatever.

At Kings County Hospital we decided to give sulfanilamide therapy a clinical trial in intrapartum infection and all cases of severe puerperal infection regardless of etiology, feeling reasonably certain that serious toxic effects could be controlled while patients were kept in bed under observation during the entire period of treatment. Vaginal swab or intra-uterine cultures were taken in many cases, but at first were not routine; blood culture was done when indicated. Since minor febrile disturbances of the puerperium are seldom caused by the streptococcus, patients with mild infection were given nothing more than supportive treatment.

It is usually difficult to outline the anatomical limits of genital tract infection from the clinical picture alone. Involvement of adjacent peritoneum, invasion of the myometrium, parametrium, or even the blood stream may occur without confirmatory evidence. The myometrial exudates which so often complicate endometritis may give no indication of their presence other than increase in the size of the uterus, or change in the character and amount of the lochia. When high fever, chills, tenderness over the uterus, pain on lateral uterine motion, pelvic masses, or peritoneal rebound pain occur, severe infection is present. Cases were classified clinically as severe because of (1) high initial rise of temperature; (2) spiking temperature: (3) peritonitis, pelvic and general; (4) chills; (5) spreading inflammation; (6) positive blood culture.

Since March, 1937, 118 patients with severe puerperal infections of the genital tract received sulfanilamide, 78 white and 40 colored; 83 infections occurred postpartum, and 35 postabortum; 46 postpartum infections or 55 per cent occurred after spontaneous delivery. Predisposing factors like parity, toxemia, placenta prævia, and abruptio need not be discussed here, nor are delivery data pertinent. However, 5 patients did have acute respiratory infection, and in the case of one patient with a suppurating paronychia, uterine culture showed Streptococcus hemolyticus, group H strain 2. Included in the postpartum group are 6 cases of peritonitis, 3 pelvic and 3 generalized, as well as 4 cases of thrombophlebitis, one with lung infarct in which blood cultures were repeatedly negative.

In the septic abortion group there were 20 patients with abdominal tenderness, in 11 of whom there was evidence of peritonitis. Chills were noted in 10 cases, and in 8 cases pelvic masses were prominent. In this group there were 2 deaths; in 1 four blood cultures were negative, and the other showed Streptococcus hemolyticus group C in each one of four cultures. Blood cultures were done in 12 cases, and uterine culture in but 9; staphylococci were found in 4 cases, Bacillus coli in 2, and streptococci in 3 cases.

TABLE I.—AMOUNT OF SULFANILAMIDE—DURATION OF TREATMENT

	to 200 grs.	200 to 400	400 to 600	600 to 800	800 to 1000	Total
to 2 days	10	1				11
2 to 4 days	5	9	5			19
4 to 6 days	5	6	9	5		25
6 to 8 days	1	8	10	11	2	32
8 to 10 days		1	12	6	3	22
10 to 12 days			3	4		7
12 to 14 days			1			1
Total	21	25	40	26	5	117*

*One patient received 1210 grs. in 14 days.

TABLE II.—CLINICAL RESULTS

Infections	Routine								
	A			B			C		
	G	D	N	G	D	N	G	D	N
Intrapartum	4	2	3	2	2		1	1	
Postpartum	9	14	2	6	3		8	6	
Postabortal	1	5		10	5	4	2	2	1

G, good; D, doubtful; N, none.

SULFANILAMIDE THERAPY

In all but 26 cases, sulfanilamide was given according to one of the following routines, usually with an equal amount of sodium bicarbonate, for 10 or 12 days, unless discontinued for good reason.

A. 80 grains a day for 2 days, 60 grains a day for 3 days, and 40 grains a day thereafter (40 cases).

B. 120 grains a day for 2 days, 80 grains a day for 3 days, and 60 grains a day thereafter (32 cases).

C. Twice routine A. (20 cases).

Often we found it difficult to maintain an even level of sulfanilamide in the blood. Titers of 11.9 after 240 grains, 18.7 after 300 grains and 3.2 after 760 grains were noted. However, fluids were not strictly controlled, nor was a 4 hour schedule of dosage maintained through the night as advocated by Long, Bliss, and Feinstone. Since we have followed their suggestion, our blood titers are consistently satisfactory. The amount of sulfanilamide given and the duration of treatment are shown in Table I.

That sulfanilamide is a powerful chemotherapeutic agent in certain types of bacterial invasion has been clearly shown, yet it is very difficult to assess the value of any form of therapy in genital tract infection. A control series of cases presenting like factors can not be set up. Colebrook and Purdie compared their results with those obtained previously. Bedside observations like rapid subsidence of fever or resolution of infective processes may be sufficiently impressive however to warrant clinical conclusions. This is not an entirely satisfactory method, but in all probability we shall never be able to do any better in this type of infection. Table II records our clinical results in 92 cases in which sulfanilamide was given in standardized dosage:

In the entire series of 118 cases, the clinical response to sulfanilamide therapy was good in 45 cases or 38 per cent, doubtful in 45 cases or 38 per cent, and there was no effect in 23 cases or 20 per cent. There were 5 deaths in all, or a 4 per cent mortality.

DEATHS

I. H., white, primipara, aged 33 years, 7 months pregnant, was admitted on January 13, 1938, with temperature 103 degrees, pulse 168. She had been ill for 10 days with fever, chills, and cough. After short labor she delivered spontaneously a stillborn fetus. The placenta was removed manually because of profuse hemorrhage. Her hospital course was characterized by high fever, rapid pulse, foul lochia, and peritonitis. Hemoglobin rose from 41 to 84 per cent as a result of 5 transfusions. Sulfanilamide was given on the second day postpartum and discontinued after 200 grains had been given. Blood culture was negative. Necropsy, 27 days after delivery, showed a pelvic abscess which had ruptured into the peritoneal cavity, generalized peritonitis, multiple abscesses of the lungs, pleurisy, and bronchopneumonia.

A. P., 18 year old primipara, was admitted to the hospital with ruptured membranes, on March 21, 1938, and delivered by low forceps after short labor. She developed a fulminating septicemia with jaundice, pelvic thrombophlebitis and signs of meningeal irritation. Three blood cultures were negative, the fourth showing Bacillus coli and non-hemolytic streptococci. Sulfanilamide was discontinued after 100 grains had been given because of a leucopenia of 3,400 on the fifth day postpartum. Four blood transfusions were given. She died on the thirteenth day postpartum.

A. C., primipara, aged 27 years, was admitted to the hospital on May 29, 1938, in labor, with toxemia

TABLE III.—TOXIC MANIFESTATIONS

	Routine A	Routine B	Routine C	Unstandardized	Per cent
Marked cyanosis	13	11	13	7	37.3
Nausea and vomiting	2	3	3	2	8.5
Diarrhea	2	1	2	3	6.8
Dermatitis					1.8
Drug fever		1	1	1	2.7
Mental reactions	2	2	4	2	8.5
Mild hemolytic anemia	5	4	2	4	12.7
Acute hemolytic anemia		2			1.8

and intrapartum infection. After 42 hours of labor she was delivered by forceps of a 10 pound stillborn fetus. Temperature rose rapidly to 103 degrees. Sulfanilamide therapy was discontinued when only 60 grains had been given, because of very marked cyanosis, hyperpnea, and diarrhea. On the fourth day temperature rose to 105.4 degrees and the patient became comatose. Blood culture showed hemolytic streptococcus. Necropsy showed gangrene of the uterus with pelvic peritonitis.

R. D., colored, primipara, aged 22 years, was admitted to the hospital on January 7, 1938, in shock, with a diagnosis of incomplete abortion. The vagina was packed and the uterus was emptied later. Chill with a rise in temperature to 104.6 degrees followed promptly. She received 365 grains of sulfanilamide. Four blood cultures were negative. She died on the nineteenth day. Necropsy revealed septic endometritis with septic thrombophlebitis of both ovarian veins.

B. R., quadripara, aged 28 years, was admitted to the hospital on August 29, 1938, with a diagnosis of incomplete abortion, temperature 102.6 degrees, and pelvic peritonitis. A few days later she bled profusely, passed some tissue, and the temperature fell to normal, later spiking and associated with repeated chills. The uterus was not entered. Large doses of sulfanilamide, totaling 1210 grains, were given in 14 days. Several blood transfusions, totaling 3700 cc. were given. Repeated blood cultures were positive for Streptococcus hemolyticus group C. Necropsy showed infected polypoid placental tissue, acute vegetative bacterial endocarditis, and a rider's thrombus at the bifurcation of the aorta. This case will be reported in detail in a later communication.

In only one of these cases was sulfanilamide therapy adequate. In 4 cases it was discontinued for what was thought to be good reason, or not begun soon enough. Probably we can not expect a good therapeutic result from chemotherapy in the presence of pelvic abscess, pelvic thrombophlebitis, retained placental fragments, and bacterial endocarditis.

TOXIC MANIFESTATIONS—TABLE III

There were no deaths due to sulfanilamide therapy. In about half of our cases some toxic symptoms appeared, occurring more often and to greater degree in those receiving the higher dosage. However, no definite correlation between the amount of the drug and the occurrence or severity of the symptoms could be made. While less than 40 grains of sulfanilamide produced toxic symptoms in some cases, in other instances more than 500 grains did not. Sulfanilamide was discontinued in 16 cases because of severe toxic manifestations.

Cyanosis possibly represents pigmentation and has nothing to do with the oxygen-carrying power of the blood. First noticed in patchy blue areas about the cheeks and lips, it rapidly becomes generalized. We have seen it occur after 20 grains had been taken, and occasionally diminish and even disappear though large doses of sulfanilamide were being given. As a rule it appeared on the second day of treatment, and persisted for 3 days after the drug had been discontinued. It may occasionally interfere with accurate determination of hemoglobin by the colorimetric method, and erythrocyte counts must be relied upon when other methods of estimation are not available.

We look upon nausea and vomiting as of gastro-intestinal origin, though it may be cerebral. Diarrhea, apparently not due to infection, has been reported by Lockwood, Coburn and Stokinger; we have noted it in 8 cases.

Signs of cerebral irritation were dizziness, 4 cases; headache, 16 cases; and drowsiness, semi-stupor, disorientation, excitement or nervousness in 10 cases. In 3 of these cases feeding was difficult.

We have found it difficult to identify drug fever beyond question in more than 3 cases. There were 9 other cases in which it appeared likely. Six of these patients were receiving large doses of sulfanilamide. The diagnosis of drug fever was made, when, after a long afebrile or low febrile period of 5 to 7 days the temperature rose without corroborative evidence of increased puerperal infection and the drug was stopped, fever abated in a day or two.

Slow anemias were common. In many cases leucocytosis diminished or disappeared during

treatment, but this was attributed to control of the infection. Acute hemolytic anemia occurred in 2 cases and yielded rapidly to treatment. Since this toxic manifestation is of great importance as it may cause death, these cases are reported in some detail:

CASE 1. W. H. was admitted on December 22, 1938, with a diagnosis of threatened abortion, 4 months. Hemoglobin was 72 per cent, Sahli; red blood cells, 3,800,000; white blood cells, 11,000; 72 per cent polymorphonuclears. Vaginal swab showed gram negative intracellular diplococci.

Bleeding stopped soon after admission, and fever occurred on December 27, rising to 103.8 degrees on December 28 and 30, with severe remissions. Four doses of sulfanilamide, each 30 grains, were given on December 30, and one dose of 30 grains the next morning, a total of 150 grains.

The next day she had a chill, became extremely toxic, occasionally disoriented, vomited, and became drowsy and jaundiced. Hemoglobin dropped to 38 per cent Sahli. Her blood showed 83 units for the icterus index, an immediate direct van den Bergh reaction, 5.0 milligrams of bilirubin, 64.2 milligrams of urea, and 194 milligrams of cholesterol. The urine of January 2 was positive for bile by the foam test. A later specimen showed a slight amount of bilirubin, increased amounts of urobilinogen, and markedly increased amounts of urobilin. The severe anemia was accompanied by marked leucocytosis, up to 60,000, and nucleated erythrocyte and immature leucocyte forms. Later reticulocytes up to 5 per cent were noted.

She aborted a macerated fetus on January 4, 1939. Jaundice, drowsiness, and vomiting continued for 3 or 4 days, subsiding slowly. Treatment included high carbohydrate, low fat diet, and repeated blood transfusions. Marked improvement occurred on January 10, and she was discharged in good condition on January 18.

CASE 2. M. C., a colored multipara, aged 30 years, was curetted on January 9, 1939, for incomplete abortion, with temperature, 100 degrees; pulse, 100; red blood cells, 4,200,000; hemoglobin, 72 per cent, Sahli. On January 11, temperature rose to 104 degrees, and 120 grains of sulfanilamide were given on that day, and the next. On the third day when 300 grains had been given, her temperature fell to normal, but hemoglobin was found to be 32 per cent Sahli, and red blood cells, 2,030,000. This severe anemia was not accompanied by nausea, vomiting, or jaundice. However, urinalysis showed increased amounts of urobilinogen and greatly increased amounts of urobilin. On January 17, icterus index was but 3 units. Repeated blood counts showed only a moderate leucocytosis, the highest 13,250, and nucleated red cells were found but once. She received two transfusions and iron medication and the hemoglobin rose to 50 per cent on January 21, when she was discharged for ambulatory treatment of the anemia. This was thought to be acute hemolytic anemia in spite of the absence of usual confirmatory evidence.

SUMMARY AND CONCLUSIONS

Those who have had considerable experience with puerperal infection know that its prognosis is grave in its severe forms. The etiology, bacteriology, and pathology of a large number of cases must be thoroughly studied before the efficacy of any remedial agent can be demonstrated. A control series of alternate cases is futile, and comparison of mortality rates with previous experience is inconclusive, though helpful. It has been clearly shown by others that sulfanilamide has specific effect in infections caused by the beta strain of the hemolytic streptococcus. Whether genital tract infection by other organisms is susceptible to the drug is not yet clear, though it would appear to be. Possible untoward effects of any dangerous remedy must be assessed under carefully controlled conditions before its use is warranted. At any rate trial of sulfanilamide therapy involves no abandonment of any established method of treatment, except possibly forced fluid intake, for there are no proved remedies for puerperal infection.

Large doses of sulfanilamide were given to 118 patients with severe puerperal infections of the genital tract, regardless of their etiology. Clinical response was prompt and satisfactory in 45 cases, or 38 per cent. In an additional 45 cases, or 38 per cent, results were not convincing, yet good enough to make us feel that the drug may have played an important part in recovery. In 23 cases, or 20 per cent, no beneficial results were observed. There were 5 deaths, a mortality of 4 per cent.

Administration is definitely associated with toxic manifestations none of which need be a serious hazard. Usually obvious and rarely severe enough to warrant discontinuance of therapy, toxicity is actually low. A moderate fall in hemoglobin is common and harmless. We have seen no case of agranulocytosis. Acute hemolytic anemia can not be foreseen or prevented since it is apparently due to idiosyncrasy, developing quickly within the first few days of treatment after comparatively small doses of the drug. Rapid drop in

hemoglobin and erythrocytes, leucocytosis, marked reticulocytosis, bilirubinemia and urobilinuria are noted. Daily blood counts for at least the first 5 days are essential. Though it occurs but seldom, and transfusion is effective, it is because of the ever present danger of serious blood changes that indiscriminate administration of sulfanilamide is inadvisable. Other toxic manifestations are readily observed clinically and subside when the drug is withdrawn.

In mild cases of puerperal infection sulfanilamide is not indicated. Certainly proper bacteriological investigation should precede therapy, but it is not essential. Intrapartum infections should be treated with sulfanilamide at once. Report on Streptococcus hemolyticus may be had in 24 hours; vaginal swab culture is better than intra-uterine. If hemolytic streptococci are found, drug therapy should be discontinued only under exceptional circumstances, and one should not be too quick to stop its administration because bacteria have disappeared or a diagnosis of drug fever has been made.

Our most recent experience indicates that optimum benefit may be expected with spaced maintenance doses of 20 to 30 grains of sulfanilamide and moderate fluid restriction, provided a large initial dose has been given the patient.

In severe puerperal infections of the genital tract whatever their etiology, sulfanilamide may be used and should be, provided the patient is in a hospital where its administration may be controlled.

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THE McCLURE-ALDRICH TEST IN WATER BALANCE FOLLOWING OPERATION

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OF recent years surgeons have become increasingly aware of the prime importance of the maintenance of a proper water and electrolyte balance in the patient after operation. In the sick, surgical patient a water imbalance is particularly liable to occur because of the unusual losses of fluid from sweating during the operation, from vomiting, from enterostomies, from draining wounds, and from excessive metabolism. Moreover, in these cases it is often impossible for a time, at least, to administer oral fluids. Coller and Maddock (4), in a careful study of 18 surgical patients, found fluid losses varying from 95 to 1,979 grams during the operative period and from 140 to 738 grams in the 4 hours immediately after operation. In further studies Coller and Maddock (7) show that the average daily loss from the sick surgical patient is from two to three times that of the normal individual in exclusion of abnormal losses due to vomiting, draining wounds, fever, etc.

Ravdin and Rhoads state:

> The results of fluid deficit are probably only partially known, but many of those with which we are familiar are particularly unfortunate at a time when the patient has just been operated upon. Unless the deficit is due to hemorrhage, there will be an increased blood viscosity which tends to slow the circulation and increase the work of the heart. The urinary output is diminished at a time when there is often an increased breakdown of protein going on due to tissue injury at the operative site and to the substitution of protein for fat and carbohydrate as food. There are often toxic products of infection or of disintegrating tissue whose chief avenue of excretion is thought to be the kidney and whose excretion may be hindered by a low urinary output. If the urinary output is cut down sufficiently, uremia will develop. The kidneys will no longer be able to control the acid-base equilibrium adequately at a time when starvation ketosis is present. If acidosis or alkalosis occurs it may incite vomiting with further dehydration, thus forming a vicious circle. Diminished salivation commonly results which often makes the patient very uncomfortable and restless, and probably predisposes him to parotitis. Hyperpyrexia sometimes appears in dehydration because the sweat glands cannot excrete enough perspiration to control the body temperature.

The usual guides in the management of water balance after operation are: (a) the clinical picture; (b) the urinary output; (c) quantitative measurements of intake and output; (d) the erythrocyte count; (e) the hemoglobin determination; and (f) the blood protein level (10). The clinical picture of dry skin and dry tongue is unfortunately too familiar. As Cutting says, dehydration should never be allowed to develop in the surgical patient to the point where it is clinically recognizable. The urinary output is an excellent guide, but may be untrustworthy when kidney function is impaired; moreover, 24 hours may be required to make an accurate determination. The quantitative measurements of intake and output as described by Coller and Maddock are valuable, but so involved as to be beyond the scope of the average hospital. The red blood count and hemoglobin are variables often influenced by blood loss occurring during operation or in the period which follows. These values are also affected by the changes accompanying dehydration, notably that of increased blood viscosity which causes a barrier to the normal capillary circulation, and the destruction of red blood cells and hemoglobin which results from severe anhydremia of several days' duration. Blood protein determinations are difficult and time taking and may be influenced by a protein deficiency which is part of the patient's general picture after operation. Blood protein is destroyed when severe anhydremia has existed several days (8).

Another factor with which we must be concerned is the electrolytic balance inasmuch as

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it is intimately bound with water metabolism and must be treated in conjunction with it. Of the electrolytes involved sodium$^+$ is the most important. Much of the fluid lost abnormally by surgical patients is rich in sodium$^+$ particularly that lost from the gastrointestinal or biliary tract. Consequently, in these patients there often results a dehydration that cannot be compensated for by water alone even though the red blood count and hemoglobin determinations return to normal and the urinary output is quantitatively sufficient. Nor is the danger of sodium$^+$ deficiency all that need be guarded against. Because of the too liberal use of physiological saline or Ringer's solution as a routine fluid for intravenous use whether sodium chloride is needed or not, an oversufficiency of sodium$^+$ is frequently brought about, sometimes to the extent that edema is clinically evident.

With these thoughts in mind a study was undertaken to determine the value of the McClure-Aldrich test as a guide to the management of water balance after operation.

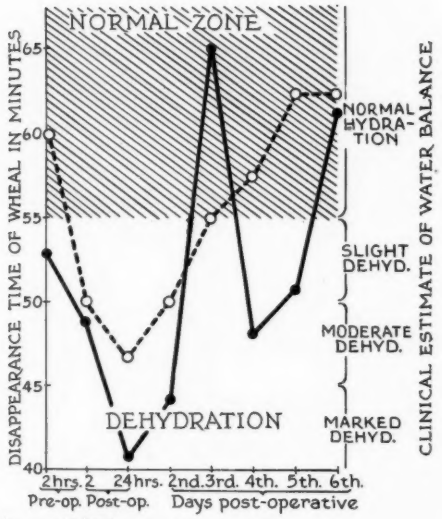
In 1923, W. B. McClure and C. A. Aldrich first introduced a test which has since borne their names, consisting of a measurement of the disappearance time of an artificial injected wheal of normal saline. The test was originally applied in cases of nephritis in an effort to determine the thirst of subcutaneous tissues and thus estimate the severity, prognosis, and progress of the disease (9). It has since received a wider application and has been used in the study of vascular disease (2, 3, 11), cardiac failure, toxemia of pregnancy, scarlet fever, and other diseases. Its use has in general been limited to those conditions in which edema plays a part, to measure the edema and detect it before it is clinically evident. Its efficiency in determining water balance under these conditions has been widely studied and proved (6). The mechanism of the test is in some dispute. The generally accepted mode of action is, however, that the disappearance of intradermal saline is due almost wholly to a dispersement of the fluid into the interstitial spaces and cells and that the length of time that this transfer takes, as measured by the disappearance of the wheal, is inversely proportional to the tissue avidity for water.

On this basis it seemed logical that the test would furnish a practical, accurate, quantitative means of measuring water balance in the surgical patient. In reviewing the literature it was found that this application was first suggested in 1927 by Appel and Brill.

In the following study the management of water balance after operation was carried out independently of the McClure-Aldrich test as a guide. Standardized equipment, including tuberculin syringes and No. 27 intradermal needles, was used throughout. All intradermal injections were made and interpreted by the same individual. In each case, when the McClure-Aldrich test was used, an average taken from multiple wheals was made. Intradermal injections of 0.2 cubic centimeter of an 0.85 per cent solution of sodium chloride were made in both forearms on the volar surface at the junction of middle and proximal thirds, care being taken to avoid superficial veins, and over the chest at points midway between the sternoclavicular joint and the apex of the anterior axillary fold. In those patients to whom intravenous fluids were administered the arm or arms affected were not used as sites of skin tests because of the fact that around the site of intravenous infusions there is usually a local disturbance of water balance.

McClure-Aldrich tests were performed in the following patients from 4 to 2 hours before operation, with 1 exception, from 2 to 4 hours after operation, and thence every 24 hours at approximately the same time each day until a near normal fluid balance was considered established. In all instances erythrocyte and hemoglobin determinations were made by the same individual at the same time the skin tests were done.

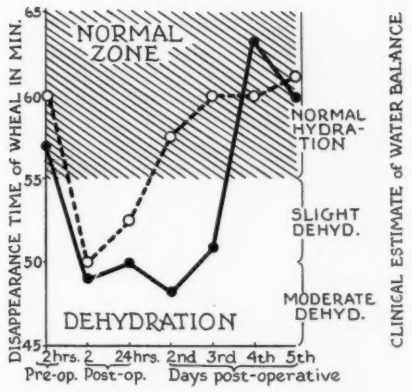
Patient G. S. (Fig. 1), a 59 year old white male, entered the Evanston Hospital on October 1, 1938, with complaints of vomiting, epigastric pain, and dizzy spells. In 1911, the patient was operated upon for perforated gastric ulcer. A gastrostomy was performed. Following this he was completely well until 1930 when typical ulcer symptoms recurred. In August, 1938, 9 weeks prior to admission he began to suffer from intermittent vomiting and progressively increasing epigastric soreness to the point of pain. During the 3 weeks prior to admission, the patient had had a daily emesis of from 500 to 1000 cubic centimeters of greenish fluid. For the last 9 weeks there had been a tendency toward diarrhea and the



Fluid intake c.cm..	(12hrs. *3250)	2600	2650	5290	2400	1950	1200
NaCl intake gm...	(12hrs. 19.5)	15.1	15.1	7.5	1.3	3.2	0
Urine c.cm.....		420	620	620	580	800	450
Urine specific gravity....		1.024	1.026	1.027	1.020	1.020	1.016
Hgb. %	103.4 100.3	107.1	103.8	97.4	94.1	97.4	97.4
R.B.C. millions	4.95 4.93	5.08	5.07	4.84	4.72	4.76	4.46

*Including 500 c.cm. of whole blood.

Fig. 1. Gastro-enterostomy on G. S., male, aged 59 years. ○---○ Clinical estimate of water balance. ●—● Disappearance time of artificial wheal.



Fluid intake c.cm.....	(12hrs. 2000)	2500	2800	4200	3910	1300	
NaCl intake gm.....	(12hrs. 6.5)	13	17	20	6.5	6.5	
Urine c.cm...		800	1000	550	1150	500	
Urine specific gravity...		1.024	1.014	1.016	1.012	1.014	
Hgb. %.....	94.1	97.4	94.1	97.4	94.1	84.4	94.1
R.B.C. millions ...	4.56	4.73	4.82	4.94	4.98	4.60	4.80
*Abnormal fluid output		300	200	600	100	0	200

*Stomach aspiration.

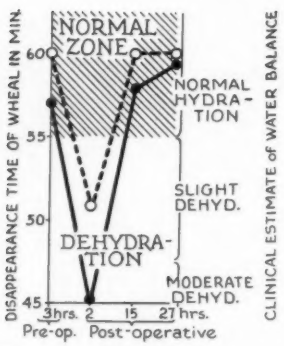
Fig. 2. Gastric resection on F. M., male, aged 45 years. ○---○ Clinical estimate of water balance. ●—● Disappearance time of artificial wheal.

stools had been black. There had been occasional transient attacks of vertigo during the last 3 weeks. There had been a weight loss of 30 pounds in the last year.

Physical examination revealed a rather thin white male who did not appear acutely ill. The abdomen presented a long midline scar. There was no tenderness or rigidity, but there was slight hyperperistalsis. Laboratory examination was negative save for the x-ray film which revealed a duodenal ulcer with a high grade of obstruction. Diagnosis: duodenal ulcer with almost complete obstruction at the pylorus.

The patient was placed under conservative ulcer management without satisfactory response. On the fourteenth day following admission a gastro-enterostomy was performed. The operating time was 2 hours. Anesthesia was by means of drop ether. The patient's condition was poor throughout the latter part of the operation. He received 500 cubic centimeters of whole blood at that time. Eight hours after operation, the temperature rose to 102.2 degrees and then declined. On the second day after operation the patient became cyanotic and his pulse became fast and weak. Nasal oxygen relieved this and on the following day he began to take fluids by mouth. Subsequent convalescence was uneventful and on October 20, 1938, the patient was discharged from the hospital.

Although this patient was hospitalized for 13 days prior to operation and clinically his state of hydration was thought to be well within normal, the McClure-Aldrich test shows that he entered the operating room with a handicap, that of dehydration. This fact was perhaps responsible for the marked dehydration indicated by the wheal disappearance time 24 hours after operation, a degree of dehydration not observed clinically. It is of interest to note the sensitivity of the McClure-Aldrich test as demonstrated by the sharp rise in the curve on the third day after operation, on which day the fluid intake had been doubled, and how abruptly the curve falls when the previous rate of fluid administration was adopted. It is quite apparent that if the wheal disappearance time had been used as a guide for fluid administration in this patient, a state of dehydration could have



Fluid intake c.cm...		o	500	1350
NaCl intake gm....		o	o	o
Urine c.cm.....		o	400	350
Urine specific gravity			1.020	1.018
Hgb. %.....	94.1	97.4	97.4	94.1
R.B.C. millions.....	4.74	4.86	4.79	4.58

Fig. 3. Herniotomy on A. A., male, aged 53 years. ○---○ Clinical estimate of water balance. ●—● Disappearance time of artificial wheal.

been prevented during the fourth and fifth days after operation.

Patient F. M. (Fig. 2), a 45 year old white male, entered the Evanston Hospital on October 15, 1938, with complaints of epigastric pain, abdominal distention, nausea, and vomiting. The onset of his present illness began in the fall of 1936 with occasional attacks of epigastric distress at mid-morning. This became progressively worse and was accompanied by nausea and vomiting. He lost 18 pounds in 3 months. Relief was obtained only by sleep. In January, 1937, 3 months after onset of symptoms he was hospitalized. A gastro-intestinal series was negative, but a stone in the left kidney and left ureteral stricture was found. A left nephrectomy was performed. Symptoms were relieved until July, 1937, when there was an attack of hematuria accompanied by passage of several small stones. Epigastric pain recurred. This time relief was obtained upon taking bicarbonate of soda. A repetition of urinary symptoms occurred February, 1938. The patient was again hospitalized and at that time x-ray evidence of gastric ulcer was found. Medical management failed to give complete relief of gastro-intestinal symptoms and the patient was advised to undergo surgical treatment. The patient had had pneumonia with pleurisy in 1935 and an appendectomy had been performed in 1913.

Physical examination showed a well nourished white male who did not seem acutely ill. There was slight epigastric tenderness. Laboratory examination showed a slight leucocytosis. Diagnosis: chronic peptic ulcer.

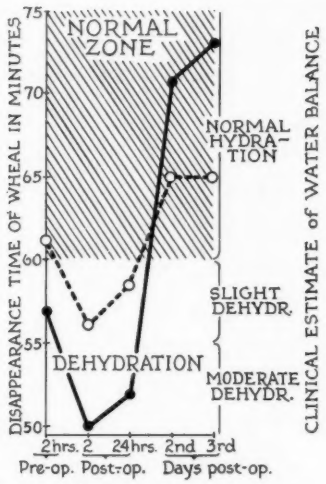
Five days following admission a gastric resection was done. Operating time was 3 hours and the patient's condition was good throughout. Anesthesia was by means of ethylene, oxygen, and ether, closed method. The patient made satisfactory progress and was discharged on November 15, 1938, in a convalescent state.

In this instance the McClure-Aldrich test demonstrated a slight to moderate dehydration which persisted through the third day after operation and was relieved only when fluid intake was increased approximately 50 per cent. On the second and third days the dehydration present was not observed clinically and thus the patient was allowed to continue in a dehydrated state 2 days longer than necessary. It is of interest to note that although the McClure-Aldrich test demonstrated a state of dehydration, the urinary output varied daily from 550 to 1000 cubic centimeters and the specific gravity was as low as 1.014. This may indicate the unreliability of urinary studies in determining dehydration when intravenous fluids are being administered at such a rate that an overflow through the kidneys occurs.

Patient A. A. (Fig. 3), a 53 year old white male, a laborer, entered the Evanston Hospital on October 5, 1938, with complaints of pain and swelling in the right groin of 7 years' duration. Onset of the present illness began 7 years ago with the appearance of a symptomless diffuse swelling in the right groin. This had become progressively more pronounced and had of late been accompanied by burning pain. Upon straining or coughing a large mass descended into the scrotum. For 3 years the patient has been aware that he had high blood pressure. It had never caused symptoms. He is now recovering from a "cold" of 2 weeks' duration.

Physical examination revealed a well developed and well nourished white male not acutely ill. The nasal mucosa was congested and the tonsils chronically inflamed. The heart was enlarged 3 centimeters to the left of the mid-clavicular line. The blood pressure was 224/124. Upon inspecting the abdomen the right external inguinal ring was found to be enlarged, admitting the index finger. A large mass protruded through this opening filling the right scrotum. Laboratory findings were essentially negative except for a mild leucocytosis and an electrocardiogram which revealed hypertensive heart disease. Diagnosis: complete indirect inguinal hernia, right, and essential hypertension with hypertensive heart disease.

Six days after admission a herniotomy was performed. The operation was of 1 hour and 30 minutes' duration during which the patient's condition was good. Anesthesia was by ethylene and oxygen, closed method. Throughout the day of operation, the patient's condition remained good. Temperature



Fluid intake c.cm...	(10hrs. 1300)	3560	1600	1400
NaCl intake gm....	(10hrs. 6.5)	13	0	0
Urine c.cm.....	0	775	1850	950
Urine specific gravity		1.026	1.010	1.016
Hgb. %.....	90.9 87.6	81.2	87.6	84.4
R.B.C. millions....	4.75 3.70	3.57	3.92	3.60

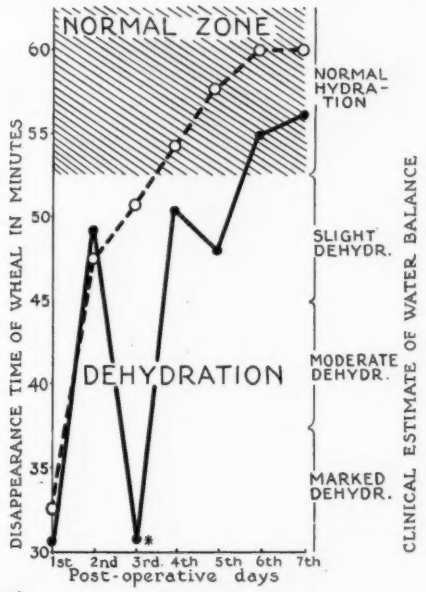
Fig. 4. Herniotomy for strangulated femoral hernia. F. S., male, aged 59 years. ○---○ Clinical estimate of water balance. ●—● Disappearance time of artificial wheal.

rose to a peak of 99.6 degrees and then declined. Satisfactory progress was maintained and on October 23, 1938, the patient was discharged.

In this simple uncomplicated herniotomy the wheal disappearance time parallels the clinical estimate of hydration, but throughout indicates slightly more dehydration than is perceptible by clinical observation.

Patient F. S. (Fig. 4), a 59 year old white male, entered the Evanston Hospital at 10:45 p.m., October 17, 1938, with complaint of severe upper abdominal colicky pain of 4 hours' duration. The pain developed insidiously, rapidly increasing in intensity, was paroxysmal and was accompanied by hyperperistalsis. There was no vomiting and bowel movements were normal. The patient was well prior to onset of above symptoms. Twenty-seven years ago the patient had a strangulated hernia with an attack similar to the present one. For the past year the patient has worn a truss for a left femoral hernia.

Physical examination revealed a well developed, well nourished white male in acute pain. The abdomen was generally tender and tense. There was moderate distention and hyperperistalsis. Laboratory examination revealed a leucocytosis of 12,100



Fluid intake c.cm.....	1600	2600	2000	2270	2420	2030	1285
NaCl intake gm.....	10.8	14.8	3.25	1.7	6.5	6.5	0
Urine c.cm..		1200	1100	2050	1475	1000	1300
Urine specific gravity...		1.012	1.012	1.006	1.009	1.012	1.012
Hgb. %.....	90.9	81.1	74.6	84.4	81.1	81.1	84.4
R.B.C. millions..	4.35	4.06	3.86	4.19	4.17	4.24	4.28

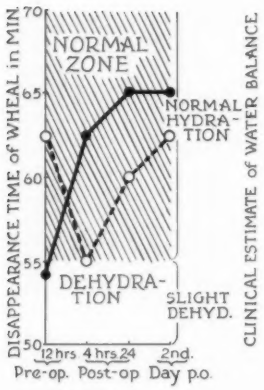
*Slight pitting edema present, attributable, perhaps, to NaCl intake of previous 24 hours.

Fig. 5. Gastric resection on M. H., female, aged 11 years. ○---○ Clinical estimate of water balance. ●—● Disappearance time of artificial wheal.

white blood cells. X-ray examination demonstrated an acute intestinal obstruction. Diagnosis: strangulated femoral hernia.

Sixteen hours after admission the patient was operated upon, the intestinal obstruction relieved, and the femoral hernia repaired. Operating time was 1 hour and 10 minutes. The patient's condition remained good throughout. Anesthesia was by means of ethylene, oxygen, and ether, closed method. The patient made satisfactory progress and was discharged on October 28, 1938.

Again we see by means of the McClure-Aldrich test, that slight dehydration was present upon onset of operation, a state of unpreparedness which could have been overcome had its presence been recognizable clinically. We see that a moderate dehydration exists for 24 hours after operation, unobserved clinically.



Fluid intake c.cm...	(16hrs. / 2870*)	1730	1800	
NaCl intake gm....	(16hrs. / 15.5)	2	0	
Urine c.cm.....		0	405	525
Urine specific gravity			1.022	1.020
Hgb. %.....	77.9	81.1	84.4	77.9
R.B.C. millions.....	3.34	4.35	4.48	3.86

*500 c.cm. of whole blood included.

Fig. 6. Resection of rectum on B. L., female, aged 70 years. O---O Clinical estimate of water balance. ●—● Disappearance time of artificial wheal.

Patient M. H. (Fig. 5), an 11 year old white female, entered the Evanston Hospital on October 3, 1938, complaining of hematemesis for 2 days, inability to retain food or water in stomach for 3 days, and weakness and thirst for 1 day. She had been perfectly well prior to the onset of symptoms 2 days previously. Physical examination disclosed a marked weakness and marked evidence of dehydration. There was bilaterally a mild cervical lymph adenopathy. In the abdomen there was found a smooth, firm, tender mass, slightly mobile, present in the upper part of the left lower quadrant. Its diameter was about 8 centimeters. Laboratory findings were essentially negative. Hemoglobin was 90.9 per cent (Haden Hauser) and red blood cells 4.39. Roentgenographic examination showed a large tumor mass encroaching on the duodenal bulb apparently intrinsic in origin. Pre-operative diagnosis: tumor of the stomach.

Twenty-three hours following admission the patient was operated upon. A wide gastric resection was performed. Operating time was 2 hours and 40 minutes and the patient's condition remained good throughout. Anesthesia was by means of nitrous oxide, oxygen, and ether, closed method. During the operation 500 cubic centimeters of normal saline and 300 cubic centimeters of whole blood were given. Throughout the day of operation the patient's condition remained good. The temperature rose to a peak of 103 degrees after operation and then declined. Convalescence was uncomplicated save by occasional nausea. On the fourth day she began taking fluids by mouth. On October 19 the patient was discharged. The pathological diagnosis was malignant leiomyoma of the stomach.

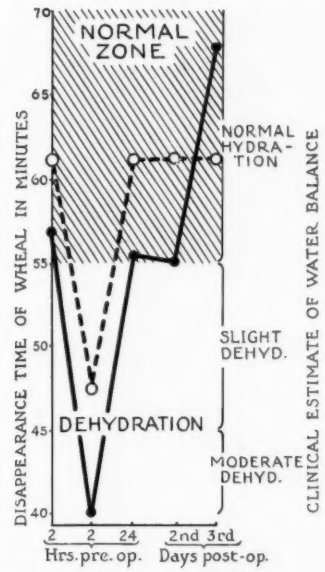
It is quite significant to note that whereas the clinical estimate and the McClure-Aldrich test almost coincide as regards the dehydration present the first and second days after operation, on the third day a marked discrepancy occurs. On that day a slight pitting edema was perceptible which we attributed to the excessive sodium chloride intake of the previous 48 hours. Indirectly relating this finding to the wheal disappearance time, it may again be emphasized that the McClure-Aldrich test is a means of measuring *tissue avidity for water*, whether that avidity is caused by insufficient water present or because the water present is in a large measure bound and unutilizable. In this instance we believe that although an excess of water was present, as indicated by edema, an excess of sodium^{+} was responsible for the fact that most of the water was bound and hence was unavailable to the tissues. When the sodium chloride intake was markedly decreased, the wheal disappearance time returned to its former level. The progressive decrease of erythrocytes and hemoglobin for the first 3 days after operation demonstrates the fact that they are of no value in estimating dehydration when bleeding is a part of the clinical picture.

Patient B. L. (Fig. 6), a 70 year old white female, entered the Evanston Hospital at 11:00 p.m., on October 17, 1938, with a present illness of 6 months' duration. In April, of 1938, she first noticed blood in the stool, a finding which has since occurred frequently. Two weeks prior to admission she began to notice a definite change in bowel habit, diarrhea alternating with constipation. Dark red blood in the stool was a constant finding. She was able to continue normal activity until the day of admission when at 6:00 p.m. she passed a large amount of blood, both fluid and clots, per rectum. In the 2 hours prior to admission she had 4 large hemorrhages per rectum.

Physical examination revealed a pale patient with a pulse of 108. There was a large cauliflower mass in the rectum revealed upon digital examination. Laboratory examination revealed a hemoglobin of 90.9 (Haden Hauser) and erythrocytes numbering 3.98. There was a leucocytosis of 17,600. Diagnosis: injected, ulcerated, primary adenocarcinoma of the rectum.

Within 2 hours following admission there were 2 additional hemorrhages per rectum. An obstructive resection was performed 10 hours following admission and opened the second day after operation. Satisfactory progress followed this, although hemoglobin and erythrocytes progressively declined to 71.4 and 3.51, respectively. On November 2, 1938, 14 days following the colostomy, a posterior resection of the rectum was done. The operation lasted 1 hour and 45 minutes. The patient's condition remained good throughout. Anesthesia was by ethylene, oxygen, and ether, closed method. Convalescence was uneventful and the patient was discharged November 27, 1938.

In this study the McClure-Aldrich test indicates, paradoxically and in direct contradiction to clinical observation, a state of dehydration present prior to operation and relieved following operation. Upon analyzing the fluid intake of the period immediately following operation, however, this is understandable. Nearly 3,000 cubic centimeters of fluids were given in the 4 hour period following operation, 500 cubic centimeters of which was whole blood. Prior to operation it is seen that a moderate grade of anemia existed. Following the 500 cubic centimeters' blood transfusion, this anemia was relieved. One may conjecture that, in addition to the total fluids supplied, perhaps the "water binding" capacity of the blood was increased thus providing a greater reservoir of water from which the tissues could draw.



Fluid intake c.cm...	(11hrs.) 1700		2450	1350	1350
NaCl intake gm....	(11hrs.) 11		11.5	0	0
Urine c.cm.....			1800	1450	600
Urine specific gravity			1.023	1.014	1.008
Hgb. %.....	81.1	87.6	81.1	84.4	84.4
R.B.C. millions....	4.19	4.36	4.27	4.38	4.15

Fig. 7. Cholecystectomy on A. G., female, aged 32 years. ○---○ Clinical estimate of water balance. ●—● Disappearance time of artificial wheal.

Patient A. G. (Fig. 7), a 32 year old white female, entered the Evanston Hospital on October 30, 1938, with complaints of pain in the epigastrium and right upper abdomen, abdominal distention with eructation, nausea, vomiting, and clay colored stools. Five years previously following the birth of her seventh child onset of the present symptoms began. Symptoms were associated with intermittent attacks of clay colored stools without evidence of jaundice. These symptoms became more severe and lately had become complicated by attacks of severe upper right abdominal pain, knife-like in character, which radiated to the right shoulder. These attacks occurred every 2 or 3 days and persisted for 3 hours. There was a history of a similar attack 15 years before.

Laboratory examination was essentially negative save for an x-ray finding of cholelithiasis. Diagnosis: cholesterosis and cholelithiasis. Physical examination revealed a well developed, well nourished white female who did not appear acutely ill. There was tenderness in the gall-bladder region. Findings were otherwise negative.

The third day following admission a cholecystectomy was performed. Operating time was 50 minutes and the patient's condition remained good throughout. Anesthesia was by means of nitrous oxide, oxygen, and ether, closed method. Convalescence was uneventful and the patient was discharged November 16, 1938.

Observation clinically and by the McClure-Aldrich test are seen to parallel each other closely, but again it is evident that by clinical estimation dehydration is underestimated.

CONCLUSIONS

1. The McClure-Aldrich test was used in 7 patients after operation in an effort to determine its value as a guide to the state of hydration and detailed reports are presented.

2. In the cases studied the McClure-Aldrich test was found to be a sensitive and reliable index to the state of hydration. It was found to be a useful guide to the optimal fluid administrations provided the electrolytic balance was taken into consideration.

3. Although this series is too small to be conclusive, the McClure-Aldrich test appears to be a valuable adjunct to the clinical appearance of the patient, to the intake and output studies, and to the blood studies in the estimation of hydration after operation.

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THE SIGNIFICANCE OF THE RADIATION REACTION IN CARCINOMA OF THE CERVIX UTERI

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PATHOLOGICAL study of material derived from the first 70 cases of carcinoma of the cervix treated in the Pondville Hospital by the method of Meigs and Dresser brought out several interesting and important observations.

The first of these throws further light on the significance of histological grading in group prognosis; the second, on the significance of histological evidence of radiation change noted in the tumor cells; third, on the significance of radiation changes in the supporting stroma of the tumors.

In most cases, a biopsy was taken before treatment; in others, after the x-ray treatment had been completed; in others, after the x-ray and radium treatment had been completed. In 5 cases no biopsies were taken at Pondville, the initial diagnosis having been established by biopsy at the hospital from which they were referred. The ideal procedure is to take the initial diagnostic biopsy, then one after completion of the x-ray treatment, one after the first radium treatment, one after the second radium treatment, and one 3 months later.

These 70 cases, when divided into clinical groups, showed 8 to fall in the A and B groups, and 62 in the C and D groups. When divided according to histological grades, we found 1 epidermoid carcinoma, Grade I; 25 epidermoid carcinomas, Grade II; 32 epidermoid carcinomas, Grade III; 4 epidermoid carcinomas, ungraded; 3 adenocarcinomas; 1 undifferentiated carcinoma; and 4 epidermoid carcinomas according to biopsies at other hospitals and were checked in this laboratory.

We have divided the cases into three grades histologically, of which Grade I is the lowest, and Grade III the highest. In Grade I we require the presence of numerous epithelial pearls, as well as a considerable degree of keratinization. Intercellular bridges must be readily visible. Mitoses average less than 2 per high power field. There is only slight variation in size and shape of the tumor cells. In Grade II, there are rare, or no epithelial pearls; a moderate amount of keratinization; some intercellular bridges; an average of 2 to 4 mitotic figures per high power field; moderate degree of variation in size and shape of tumor cells. In Grade III there are no epithelial pearls; there is only slight evidence of keratinization; intercellular bridges are not distinguishable; mitoses average over 4 per high power field; there is often marked variation in size and shape of tumor cells, with numerous tumor giant cells. Occasionally, the tumor cells may be small, elongated, and closely packed.

In estimating the presence and degree of radiation reaction of both stroma and tumor cells, we have used two main categories—moderate radiation reaction, and marked radiation reaction. In case of a moderate radiation reaction shown by the tumor cells, the following points are required: (1) a diminution of mitotic activity, (2) some necrosis, (3) some vacuolization of cytoplasm, (4) in spite of these changes, the tumor is still readily recognizable.

For a marked reaction: (1) Mitoses are very rare, or absent; (2) there is much necrosis; (3) practically all the cells are abnormal, either vacuolated, markedly distorted, or swollen with large, hyperchromatic nuclei; (4) only scattered tumor cells, or small clusters present.

For a moderate radiation reaction in the stroma, we have required: (1) the presence

From the Pondville Hospital, Massachusetts Department of Public Health.

TABLE I.—SIGNIFICANCE OF EXTENT AND HISTOLOGICAL GRADE OF TUMOR BEFORE TREATMENT

Clinical classification	Grade I			Grade II			Grade III			Not graded			Adenocarcinoma			Miscellaneous			No.
	No.	Result		No.	Result		No.	Result		No.	Result		No.	Result		No.	Result		
		Living	Dead		Living	Dead		Living	Dead		Living	Dead		Living	Dead		Living	Dead	
A	0	—	—	3	3	—	0	—	—	2	2	—	0	—	—	0	—	—	5
B	0	—	—	1	1	—	2	1	1	0	—	—	0	—	—	0	—	—	3
C	1	—	1	17	7	10	21	7	14	1	—	1	2	2	—	1—ca. simplex 2—outside biop.		1 2	45
D	0	—	—	4	—	4	9	1	8	1	—	1	1	—	1	2—outside biop.		2	17
Total	1	—	1	25	11	14	32	9	23	4	2	2	3	2	1	5		5	70

TABLE II.—DEGREE OF RADIATION REACTION OF TUMOR AFTER X-RAY TREATMENT—CORRELATED WITH END-RESULT

Radiation reaction	Living	Dead	Totals
Moderate	10	18	28
Marked	10	14	24
None	1	9	10
No tumor present	1	2	3
No biopsy	2	3	5
Totals	24	46	70

TABLE III.—DEGREE OF RADIATION REACTION ON TUMOR AFTER X-RAY AND RADIUM TREATMENTS

Radiation reaction	Living	Dead	Totals
Moderate	3	7	10
Marked	10	19	29
None	0	5	5
No tumor	5	6	11
No biopsy	6	9	15
Totals	24	46	70

TABLE IV.—DEGREE OF RADIATION REACTION NOTED IN STROMA AFTER X-RAY TREATMENT.

Radiation reaction	Living	Dead	Totals
Moderate	14	19	33
Marked	6	11	17
None	2	10	12
No stroma	0	3	3
No biopsy	2	3	5
Totals	24	46	70

TABLE V.—DEGREE OF RADIATION REACTION IN STROMA AFTER X-RAY AND RADIUM TREATMENTS

Radiation reaction	Living	Dead	Totals
Moderate	6	10	16
Marked	10	17	27
None	0	7	7
No tumor	6	7	13
No biopsy	2	5	7
Totals	24	46	70

of mild telangiectasis, or thrombosis; (2) slight increase of fibrosis; (3) mild hyalinization of collagen; (4) in the later period following radiation, slight thickening of arteriolar walls and those of venules, with hyaline deposition.

For marked reaction, we have required: (1) a marked thickening of vessel walls, with hyaline deposition, or actual necrosis of the walls with thrombosis; (2) an appreciable increase in fibrosis; (3) marked hyalinization of the collagen, sometimes with foci of necrosis.

We have based the determination of necrosis in the tumor cells on: (1) acidophilic staining of the cytoplasm, and indefiniteness of that staining; (2) pyknosis of nuclei, or loss of nuclear material; (3) karyorrhexis; (4) invasion of cells by polymorphonuclear leucocytes; (5) loss of cell membranes.

Certain alterations in the tissues resembling radiation reaction must be guarded against. These are cellular, chiefly cytoplasmic swelling due to contact of the tissues with hypotonic fluids after removal of the biopsy specimen; and intercellular, chiefly the hyalinization of collagen and of vessel walls as a result of physiological aging of the tissues or of previous cauterization. After some experience, they may be largely eliminated as a source of error.

In Table I, the clinical and histological grades, and percentage of deaths and survivals are presented. It will be seen at once that there are too few cases in Grade I and

the miscellaneous group to be of significance. However, in Grade II, 44 per cent of the patients survived, as against 28 per cent for Grade III, indicating that the group prognosis is slightly better in the lower histological grades.

The clinical grouping has definitely greater significance, only 1 patient in 8 dying in the A and B groups, and 74 per cent of the C and D groups being dead at the end of the 5 year period. It may be concluded that clinical is far more important than histological grouping.

While the grading of the initial biopsy is not of prognostic value for the individual, either from the standpoint of immediate response to radiation or of ultimate survival, the post-radiation biopsies are most helpful.

Even the biopsy immediately after the series of x-ray treatments is helpful (Table II). All but one of the cured patients showed a definite radiation reaction of the tumor cells. Ninety per cent of the group without evidence of radiation reaction died, whereas 64 per cent of those showing a moderate reaction died, and 58 per cent of these showing a marked reaction.

The response after x-ray and radium treatments is similar (Table III), all those without reaction dying, as well as 7 in 10, or 70 per cent, and 19 out of 29, or 66 per cent, respectively, of those with moderate and marked reactions.

The stromal response following x-ray treatment is of almost equal value (Table IV): 10 of 12, or 87 per cent, of those without reaction dying, whereas 19 of 33, or 58 per cent, of those with moderate reaction, and 11 of 17, or 65 per cent, of those with marked reaction died.

Following both x-ray and radium treatment (Table V), there are no survivors in the group without stromal reaction, 10 of 16, or 63 per cent, dead in the group with moderate reaction, and 17 of 27, or 63 per cent, dead in the group with marked reaction.

The biopsies are undoubtedly fairer samples of the radiation response than is often the case, as in this group the radiation is unusually evenly distributed through the tissues.

SUMMARY AND CONCLUSIONS

1. The histological grade is of less importance in prognosis than the clinical classification.

2. The response to radiation of either tumor cells or stroma is a definite guide to radioresistant cases; practically all those failing to show radiation changes on the early biopsies die of their carcinoma in spite of intensive radiation therapy. We believe such cases should be treated surgically.

3. Absence of radiation reaction in the biopsies indicates a strong probability of ultimate death of the patient from the cancer.

MULTIPLE MYELOMA

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THE disease, multiple myeloma, has long been recognized as an entity. On November 1, 1845, Henry Bence-Jones received this note from Watson with a test tube containing a thick yellow semisolid substance: "The tube contains urine of very high specific gravity; when boiled it becomes highly opaque. On the addition of nitric acid it effervesces, assumes a reddish hue, becomes quite clear but as it cools assumes the consistence and appearance which you see; heat reliquefies it. What is it?" Watson and MacIntyre sent him many specimens from which he isolated an oxide of albumin which on ultimate analysis was found to be the hydrated deutoxide of albumin.

In 1846 there appeared a report on the examination of two lumbar vertebræ and a rib affected by "mollities ossium" by Dalrymple. He stated: " . . . the disease appears to have commenced in the cancellated structure of the bone for the external osseous laminæ are firmer and more healthy than the internal. . . . The smoother surface of the rib, however, is raised by internal growths elevating the outer laminæ here and there into irregularly sized and rounded dark red projections visible through the periosteal covering. The outer layers are steel hard requiring the exertion of some force to cut them; they are thin, however, and, when sliced, expose large cancellous cavities filled by a red gelatiniform substance threaded here and there by fine bony fibers. It is in these fibers of still existing bone that many of the more important morbid changes may be witnessed."

These gentlemen deserve the credit for first describing the disease, although they considered the lesion one of "mollities ossium." However, von Rustizky, in 1873, was the first to describe the disease under the name "multiple myeloma" and Kahler, in 1899, was credited with the first description of multiple myeloma in connection with the excretion of Bence-Jones bodies in the urine. Wright first described the cells of multiple myeloma as plasma cells and proposed the name "plasma cell myeloma."

Since then, several papers and numerous reports of cases have been recorded in the literature, all of which discuss the clinical and pathological picture which is fairly well known. However, a good many cases are not what might be called typical and these variations from the so called typical case give the most difficulty in diagnosis. Knowledge of the condition has increased steadily until, now, there may be found in the literature many excellent articles setting forth our knowledge of the disease. However, the etiology of the disease is still obscure and any effective treatment may be said to be unknown. One must admit, however, that recognition of the disease is very important from the standpoint of offering the patient an accurate prognosis. Such a diagnosis often can be made in fairly advanced cases by recognition of the multiple small punched out areas in the vertebræ, ribs, skull, and pelvis on roentgenological examination (Figs. 1 to 4). However, there are many variations from the typical clinical and roentgenographical picture and, often, all other findings are negative or are not sufficiently significant to be of any help in diagnosis.

Our object in conducting this review was to discover, if possible, any facts that could add to our diagnostic acumen when confronted with a case of this disease.

It is probably true that most cases cannot be recognized until a fairly advanced stage of the disease has been reached. There are no symptoms which are pathognomonic of the disease. The most frequent and usually the first complaint was backache; in some, this was definitely localized but, in others, it was

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vague and ill defined. Early roentgenological examination in a large number of those cases gave little, if any, evidence of bony change to account for the pain, frequently very severe, from which those patients suffered. In marked contrast with this, we were astonished to observe patients having extensive areas of destruction of bone in the skull and ribs, continuing to lead comparatively comfortable lives with little limitation of their activity or derangement of their general health. Tumefaction as an early indication of myeloma occurred rarely and only in cases in which the tissue affected occupied a superficial position.

In our series, neurological signs owing to root pressure with pain referred to the abdomen and legs were noted in 2 cases of paresis of the limbs and urinary bladder. The terminal stages usually were ushered in by rapid loss of weight, progressive weakness, and a severe degree of anemia. Death resulted from inanition, uremia, and other profound toxemia.

In many instances the laboratory findings are negative and therefore are of no help. The finding of Bence-Jones proteinuria may be a lead but it must always be remembered that, in many cases of multiple myeloma, examination of the urine for Bence-Jones protein gives negative results and, so far as we know, Bence-Jones protein may never appear in the course of the disease. Thus, there are often only two alternatives: first, to suspect the disease and ask the patient to return for re-examination 3 or 4 months later when a sufficient change in the pathological picture may have taken place to make the diagnosis obvious, and second, to perform a biopsy. The presence of myeloid immaturity in the blood smear, associated with a greasy appearance as described by Watkins, although not pathognomonic, if associated with other findings is strongly indicative of involvement of bone marrow and frequently of the presence of multiple myeloma.

Between January, 1924, and January, 1937, a diagnosis of multiple myeloma was made in 120 cases at The Mayo Clinic. In reviewing this group of cases, all available records and roentgenograms have been re-examined. Of the 120 cases, we have discarded 34 in which the diagnosis did not seem certain enough to be included on the basis of recorded facts. Thus, we have 86 cases remaining from which we have drawn the following study. In order to simplify the findings we have divided this group of 86 cases into 5 groups as follows:

Group A: 19 cases in which the diagnosis was proved by postmortem examination, biopsy or both.

Group B: 53 cases in which the diagnosis has been made on the basis of clinical and roentgenological findings.

In both group A and group B all patients have died.

Group C: 5 cases in which the diagnosis was made on clinical and roentgenological evidence.

No follow-up report has been received from any one of these patients. One may assume that all of these patients are dead.

Group D: 6 patients proved by biopsy to have multiple myeloma are still alive.

Group E: 3 patients still alive 1 year or more after the original diagnosis was made. The diagnosis was made on the basis of clinical and roentgenological findings; a biopsy was not performed.

An intensive follow-up system was employed in which data were obtained from the patients or their relatives, the family physicians and the district clerk, if other sources of information were not available. In only five cases were we unsuccessful in obtaining information.

GROUP A

All 19 patients included in this group were proved to have multiple myeloma. Thirteen cases were diagnosed by biopsy, 3 were proved at necropsy and the remaining 3 were proved by both biopsy and postmortem examination. Fifteen patients were men and 4 were women. In 9 cases, pathological fracture could be demonstrated (47.3 per cent). Bence-Jones proteinuria was found in 6 of the 17 cases in which the determination was made (35 per cent) and, in one other, Bence-Jones protein was discovered in the blood, later disappearing, but at no time was there any evidence of Bence-Jones bodies in the urine. Renal dysfunction, or nephrosis, was found in 14 cases of the group (73.6 per cent). An estimation of the albumin-globulin ratio was

Fig. 1. a, left. A woman, aged 58 years. Typical appearance of multiple myeloma. Patient had Bence-Jones bodies in urine; b, humerus of same patient showing same type of lesion as is seen in skull.

Fig. 2. A man, aged 62 years. Symptoms for 1 year. Biopsy showed multiple myeloma. Roentgenogram shows involvement of tibia and femur.

made in 3 cases only with normal findings and without a suggestion of a reversal.

Owing to the presence of one unusually young individual in this group, the average age for the group is 47 years. However, it should be noted that there are only 4 patients of the group less than 40 years of age and that the largest group of any decade is 6 cases between the ages of 50 and 60 years.

The average duration of the disease from the apparent time of onset to death was 26.8 months, the shortest duration, 5 months, and the longest, 55 months. The average duration of the disease from the time biopsy was performed to death was 14.05 months. The shortest duration was 1 month and the longest, 38 months.

The sites of the lesions at the time of examination at the clinic, as far as we were able to determine from available roentgenograms, were as follows: vertebræ, 19 cases; skull, 11; ribs, 9; femurs, 8; humerus, 5; scapulas and clavicles, 3; tibias, 2; and radius, 1 case. We should point out the fact that in many of these cases it was not possible to make complete roentgenological studies; therefore the foregoing figures are not complete. We would also point to the fact that, ultimately, the involvement in many of these cases must have been more extensive than these figures indicate. Regarding the significance of evidence of renal irritation, the presence of definite renal damage has long been recognized. Its significance is, perhaps, not well understood. Bannick and Greene said that renal damage is "the result of destructive processes in the kidney, either tubular destruction with subsequent fibrosis or pyelonephritis."

The incidence of Bence-Jones proteinuria in these cases should be noted. Usually, quoted statistics show a higher incidence, 65 to 70 per cent. Why we found such a low incidence in this group cannot be explained easily. In these cases, the determination of Bence-Jones proteinuria was recorded in 17 cases. In 6 of these, Bence-Jones proteinuria was present and in 11 a negative reaction for Bence-Jones proteinuria was obtained. Thus, in the cases in which the determination was carried out 35 per cent gave positive evidence of Bence-Jones proteinuria. A positive test for Bence-Jones protein in the blood was obtained in 1 case in which examination of the urine gave negative results for Bence-Jones proteinuria. Regarding the significance of Bence-Jones proteinuria, the fol-

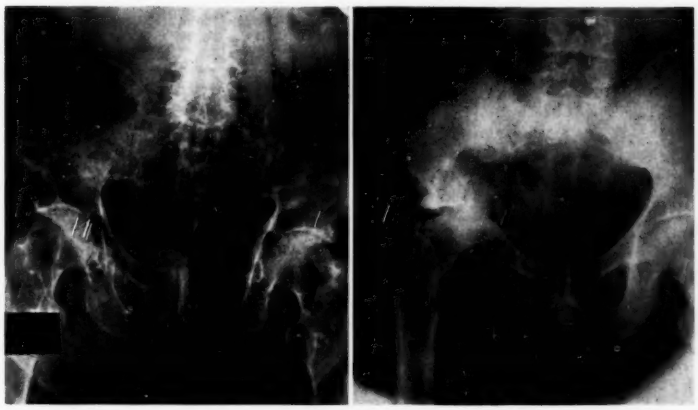

Fig. 3, left. A man, aged 40 years. Extensive lesion of spine, pelvic bones, and femurs proved by biopsy to be multiple myeloma.
Fig. 4. A man, aged 38 years. Pathological fracture of right acetabulum 1 year previous to admission. Biopsy showed multiple myeloma.

lowing facts are gleaned from some conclusions of Magnus-Levy in a paper published on this subject in 1932: The output of Bence-Jones protein in the urine is dependent on nitrogenous changes. It is not exclusively an end product. In cachectic states it may disappear from the urine. The usual serum proteins can disappear from the urine in the presence of a severe degree of Bence-Jones proteinuria. In cases of proteinuria without myeloma, the marrow is usually diseased. The amount of Bence-Jones protein lost by way of the urine is seldom more than 1 gram a day. Proteinuria is absent in 20 to 25 per cent of cases of myeloma. Bence-Jones protein may be found in the blood and in exudates but in lesser amounts in the bone marrow. Bence-Jones protein is usually formed in the bone marrow. Formation of protein in other tumors is not so high as it is in cases of myeloma. Normal marrow possibly can produce Bence-Jones proteinuria.

Table I contains data available concerning various constituents of the blood in these cases. Unfortunately the data are only fragmentary and were not consistently obtained in all cases. The fact that there are 19 proved cases of myeloma makes them worth publishing, however. If a concentration of hemoglobin of 80 per cent or less (Dare) is considered as indicative of anemia, there were 11 cases of anemia in the series.

GROUP B

All of the members of this group have died. We cannot be absolutely certain of the diagnosis because positive proof was not obtained. However, the clinical and roentgenological evidence was significant enough and make us feel that the diagnosis was accurate. Forty patients were men and 13 were women. The largest number of men were between the ages of 50 and 60 years whereas the largest number of women were between the ages of 60 and 70 years. The longest duration of life from the time the diagnosis was made until death was 4 years; the shortest duration of life was 3 weeks. Calculating the duration of life from the onset of symptoms until death, the interval varied from 3 months to 10 years. Bence-Jones proteinuria was found in 34 cases (64 per cent). In 16 cases (30 per cent), a pathological fracture could be demonstrated in the ribs or vertebræ. A history of injury was obtained in 14 cases. Nephrosis or nephritis was present to an extreme degree in 32 cases (60 per cent).

In addition to these findings there were noted: (1) an increase in the concentration of uric acid in the blood in 3 of the 4 cases in-

TABLE I.—AVAILABLE DATA CONCERNING THE BLOOD

Investigation	Case**														
	1	2	3	5	6	8	9	10	11	12	13	14	17	18	19
Serum sulfates (normal: 3–5 mg. %)	4.8												31.6* 5.7		5.2
Urea (normal: 10–40 mg. %)	44					20	20	22	63	28			290 339 32		30
Calcium (normal: 9–11 mg. %)	9	13.9		9.8	10.7		9.8		9	9.2	10.1	11.3	9.9		10.5
Phosphorus (normal: 3–4 mg. %)	3.4	2.7		3.8	2.4		3.3		4	4.7	3	4	35		6.4
Phosphatase (normal: 5 units or less; children higher)	3.5								2				5.8		2.9
Blood chlorides (normal: 570–620 mg. %)		420						627	616						
Coagulation time (normal: 6–10 min.)			10½												
Bleeding time (normal: 3 min. or less)			3												
Serum albumin (normal: 3–6 mg. %)				3.4											
Serum protein (normal: 6–8 mg. %)				11.3 gm.			6.5						6.98* 5.4		6.9
Carbon dioxide combining power (normal: 53–65 vols. %)								64.5	46						12
Sedimentation rate (normal: less than 20 mm. per hr.)								28					58(1) 98(2)		
Creatinine (normal: 1–2 mg. %)													9.6* 10.4*		10.4

*Terminal readings.
**In Cases 4, 7, 15, and 16 the special investigations itemized in this table were not carried out.

vestigated; (2) an elevation of the sedimentation rate in 5 of the 8 cases investigated; (3) the albumin-globulin ratio was reversed in 5 of the 7 cases investigated; (4) a definite lowering of the blood cholesterol was found in 2 of 3 cases; (5) the concentration of creatinine was elevated more than 2 milligrams per 100 cubic centimeters in 4 of the 6 cases investigated; and (6) serum protein was elevated more than 9 milligrams in 4 of 11 cases.

The bones involved in this group of cases were as follows: vertebræ, 36; pelvis, 29; skull, 39; ribs, 23; femurs, 14; humerus, 10; scapulas and clavicles, 18; tibias, 2; radius, 2; sternum, 2; maxilla, 1; ulna, 1; and bones of the hand, 1.

GROUP C

The absence of follow-up records in this group makes the available statistics of questionable value. One may presume that the patients of this group are dead. The following facts are noted: the group contained 4 men and 1 woman whose ages ranged between 40 and 70 years; the average age for the group was 57 years.

GROUP D

The 6 members of this group are alive. The presence of multiple myeloma was proved by a biopsy in each case. For these reasons these cases have been checked more carefully than those of other groups. A brief summary of each case seems worth recording.

CASE 1. A woman, aged 20 years, had experienced pain for 6 months and paraplegia for 5 months. Laminectomy was performed and a tumor was removed and diagnosed as myeloma by the pathologist. Recovery did not occur but the patient was alive 21 months after the onset of symptoms.

CASE 2. A man, aged 62 years, 16 years ago noticed huskiness of his voice. Roentgen therapy was given with improvement. The huskiness recurred 2 years before admission. An ulcer was found on the pos-

terior surface of the tongue and was diagnosed as myeloma. Since then, he has been in good health (2 years). Evidence of involvement of bone could not be found.

CASE 3. A man, aged 41 years, 4 months before admission noticed puffiness over his left eye and swelling of the left side of his head. Roentgenological examination gave evidence of a large area of destruction in the skull. A tumor was removed together with the overlying skull and dura, which on histological examination proved to be a myelocytoma. He is now apparently well, 29 months after the operation.

CASE 4. A woman, aged 46 years, had a tonsillectomy performed 3 months before coming to the clinic. She later had a tooth extracted but swelling of the cheek persisted. On admission to the clinic a destructive lesion of the antrum was discovered as well as lesions of the skull, pelvis, and femurs. Biopsy of the antral lesion showed it to be a multiple myeloma. Deep roentgen therapy was given, and the patient was last reported to be in good condition, 21 months after the onset of the symptoms.

CASE 5. A woman, aged 53 years, on her first admission to the clinic, gave a history of backache of 3 years' duration and of sciatic pain of 1 year's duration. Roentgenological examination gave evidence of extensive destruction of half of the sacrum with some suggestive lesion of the skull. A diagnosis of multiple myeloma was made. Roentgen therapy was given and the patient returned to the clinic almost 2 years later. At this time there was roentgenological evidence of only slight extension of the destructive process: thus, a biopsy was performed and the lesion was found to be a multiple myeloma. She is still alive 5 years after onset of the symptoms.

CASE 6. A man, aged 38 years, first reported at the clinic in December, 1930. He complained of pain in the chest of 1 year's duration and weakness and stiffness of one leg of 3 weeks' duration. Roentgenological examination gave evidence of partial destruction of the fifth dorsal vertebra and, on account of the paraplegia, a laminectomy was done and a multiple myeloma was found. Roentgen therapy improved his condition. He is still alive (8 years) but has had another laminectomy performed elsewhere, and the diagnosis has been confirmed again by pathological study.

Analyzing these cases, we would say that the patient reported first in this group has probably only a short time to live; the second patient had an unusual type of myeloma which may never affect the bones; the third patient probably is not cured; the condition is merely temporarily arrested. The same may be said of the fourth patient; the fifth and sixth patients undoubtedly have true multiple myeloma of exceptionally long duration, 5 years and 8 years, respectively.

TABLE II.—SEX AND AGE DISTRIBUTION

	Cases
Males	63
Females	23
Total	86

	Years
Average age (men)	52
Average age (women)	49.6
Youngest patient (boy)	4
Oldest patient (man)	75

Duration of disease from onset—
4 months to 5.25 years; average, 26.9 months.

There are not sufficient laboratory data available in this group to make any tabulations worth while. The last 2 cases are of principal interest because of the apparently long duration of the disease. It should be noted that of these 6 cases only one had Bence-Jones proteinuria. Both of these patients received considerable roentgen therapy which may account, in part, for their prolonged existence.

In summarizing the findings in our entire group we have tabulated the incidence of the disease according to sex and age with the duration of the disease (Table II). The average duration of the disease, 26.9 months, approximates the average for the subgroup of proved cases, 26.8 months. Table III is a summary of the data concerning constituents of the blood, some of which are reputed to be of help in the diagnosis of multiple myeloma. Although there are many variations from the normal among these findings it is doubtful that any can be considered more than a help in making the diagnosis.

As we have said before, Bence-Jones proteinuria, although suggestive, was present in only 51 per cent of the entire group of cases. Most of the other findings of significance point toward renal damage which is probably present in all cases before death ensues. It cannot be said that such renal damage is always caused by the excretion of Bence-Jones protein by the kidney because we have evidence of renal damage in at least 61 per cent of the cases, whereas Bence-Jones proteinuria was found in only 51 per cent of the cases.

The albumin-globulin ratio does not seem to be a test on which much reliance can be placed because, in our series, the ratio was

TABLE III.—SUMMARY OF DATA CONCERNING CONSTITUENTS OF BLOOD IN ENTIRE SERIES

Investigation	Number of estimations	Results		Normal findings
			%	
Albumin globulin ratio	10*	Reversed	50	1.5:1 to 3:1
Carbon dioxide combining power	8	All normal		53–65 vols. % (adults) 40–50 vols. % (children)
Blood chlorides	6	All normal		570–620 mg. %
Uric acid	4	3 elevated	75	2–4.5 mg. %
Blood cholesterol	3	2 reduced		160–200 mg. %
Blood calcium	37	Elevated	18.9	9–11 mg. %
Blood phosphorus	33	Elevated	9	3–4 mg. %
Blood phosphatase	13	Elevated	23	5 units %
Serum sulfates	13	Elevated	15	3–5 mg. %
Serum proteins	15	Elevated	40	6–8 mg. %
Blood urea	38	Elevated	23.6	10–40 mg. %
Sedimentation rate	11	Elevated	72.2	Less than 20 mm. per hr.
Blood creatinine	7	Elevated	42.8	1–2 mg. %

*Three of these are included in Group A.

reversed in only 50 per cent of the cases and in the series of proved cases none were positive, although only three estimations were made. The same may be said of calcium, phosphorus, phosphatase, and the determination of basophilia or eosinophilia, all of which are not consistently changed.

PROGNOSIS

Although there are 2 patients alive 5 and 8 years, respectively, after the onset of the disease, the outlook for these patients who have involvement of the bone is uniformly poor. In 1 case in this series, involvement of the soft parts only may be cured, but sufficient time has not elapsed since the operation to make any such statement valid. All patients who have involvement of the bone, however, almost certainly may be expected to die from this disease.

In spite of the statement by Coley that "The prognosis in multiple myeloma is by no means so hopeless as is universally believed," we have found little in the study of this series of cases to make us change our view from that expressed by Meyerding regarding the ultimate fate of these cases. Without doubt, in some cases, roentgen therapy may prolong the life of patient, but, in many instances, it seems ineffective, perhaps because the disease is so widespread when treatment is commenced. In one instance in the series, the initial lesion was cleaned out thoroughly and was treated with radium but without any apparent arrest of the disease. The prognosis, therefore, may be said to be uniformly poor, but in some cases, the disease tends to be more or less arrested by the use of roentgen therapy.

The application of therapeutic measures in the treatment of multiple myeloma is doomed to failure from the beginning. Undoubtedly, however, in a large number of cases an apparent temporary recovery has occurred from the use of roentgen therapy and tonic remedies. Although not absolutely characteristic, these periods of temporary improvement with remission of symptoms, both subjective and objective, are an interesting feature of this disease. In some of our cases an apparent osseous recovery has been demonstrated roentgenographically; that is, union of a pathological fracture has been observed with, as well as apart from, treatment. In reviewing all our cases we have gained the clinical impression that, with the use of roentgen therapy, many of our patients have experienced considerable temporary alleviation of their symptoms, but we are very doubtful that life is prolonged to any appreciable extent by this method.

In summarizing the diagnostic facts regarding myeloma, the average patient is near or past middle age and complains of severe pain in the back usually of a few months' duration. On roentgenological examination there is found some evidence of involvement of one or more vertebræ; the roentgenographic appearance may be characteristic, that is, giving evidence of small, punched out areas. The same type of involvement occurs in the bones of the skull. Bence-Jones proteinuria might or might not be found as well as other changes noted in Table III mostly pointing toward some renal damage. However, we would again emphasize the fact that there are many variations from this more or less classic picture and that the final diagnosis in many cases can be made only by biopsy, which seems to us justified in cases in which there is sufficient reason to suspect the presence of the disease.

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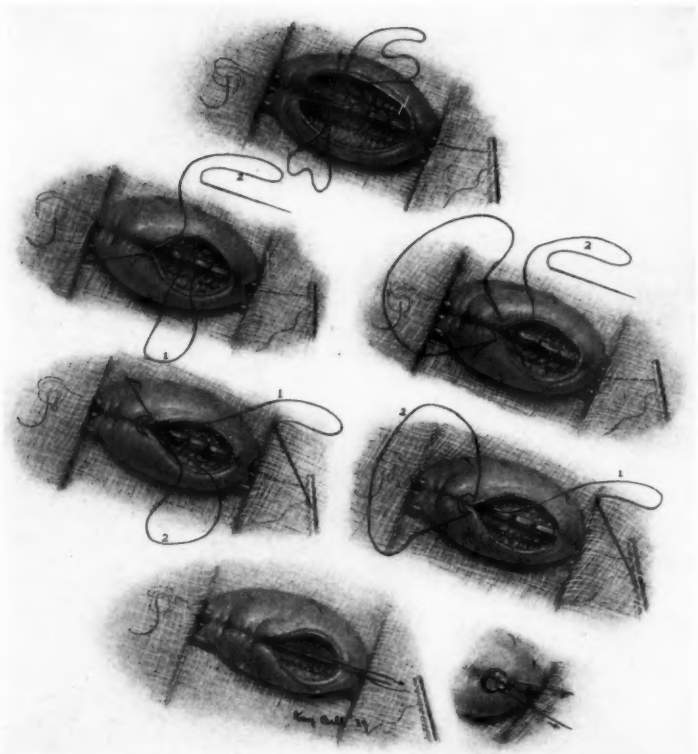

Fig. 3. This shows the steps in the placing of the inner rows of sutures. A shoemaker's type of suture is used in the posterior row and a Connell suture in the anterior row. Both sutures are hemostatic and approximate serosa to serosa.

Technique of Gastrojejunostomy Using a Crushing Clamp.—Thomas G. Orr.

CLINICAL SURGERY

FROM THE UNIVERSITY OF KANSAS HOSPITALS

TECHNIQUE OF GASTROJEJUNOSTOMY USING A CRUSHING CLAMP

THOMAS G. ORR, M.D., F.A.C.S., Kansas City, Kansas

THE stomach and jejunum are approximated by rubber-shod hemostatic clamps. The first row of seromuscular sutures of fine silk are placed as interrupted or continuous Lembert sutures. This suture line should be about 7.5 centimeters long. If a continuous suture is used a "switchback" stitch is made every second or third suture for firm fixation. When this suture is completed the needle end is concealed beneath the wound draping to be used later for the anterior seromuscular suture.

Stab wounds are made in the stomach and jejunal walls about 0.5 centimeters from the side and 1 centimeter proximal to one end of the suture line. The stab wounds are made just large enough to admit the blade of a medium sized Payr clamp. The full thickness of the stomach and jejunal walls are crushed a distance of about 5 centimeters parallel to and 0.5 centimeters from

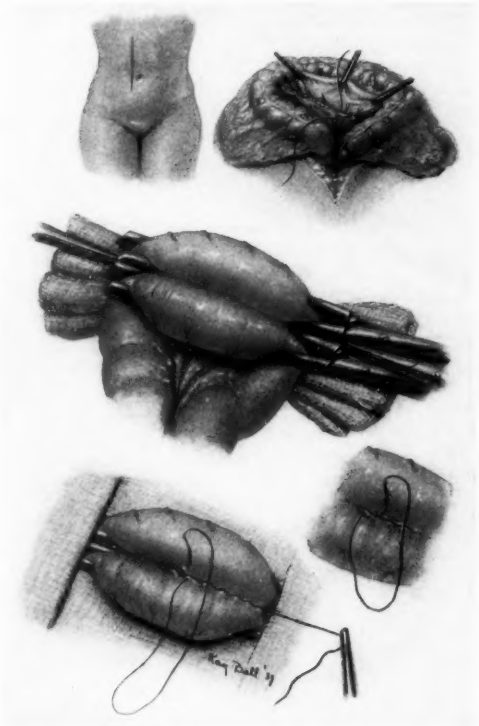

Fig. 1. The first steps in the operation are shown including location of abdominal incision, suture of mesocolon to posterior stomach wall, application of rubber-shod hemostatic clamps, and first seromuscular continuous suture.

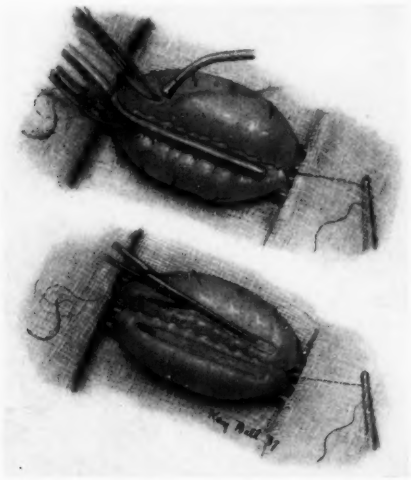

Fig. 2. Stab wounds are made in the walls of the stomach and jejunum through which a Payr clamp is passed to crush the walls along the line of incision. The stomach and jejunum are opened with scissors along the midline of the crushed tract.

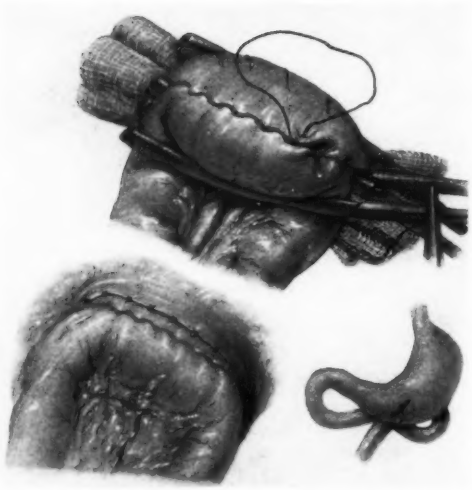

Fig. 4. The hemostatic rubber-shod clamps are loosened before the anterior seromuscular sutures are inserted. Suture of the mesocolon to the stomach and the position of the gastrojejunostomy stoma are shown.

the suture line. The crushed tract is divided along its midline with scissors. The openings in the stomach and jejunum have sealed margins as a result of agglutination of the tissues by the crushing clamp.

Through-and-through sutures of the shoemaker's type are then placed as the second or inner row. Every second suture is tied to add security to the closure. This suture approximates serosa to serosa and is hemostatic. No. 0 chromic catgut with a needle swedged on each end is used. The anterior inner row of sutures are placed by the Connell method. This also approximates serosa to serosa. The silk suture is picked up and the anterior seromuscular row of sutures is placed in the same manner as the posterior.

The use of the Payr crushing clamp agglutinates the tissues permitting a clean cut wound, minimizes oozing, makes excision of redundant jejunal mucosa unnecessary, and permits accurate approximation of serosa to serosa without difficulty. The Payr clamp may also be used in like manner in other types of intestinal anastomosis.

The accompanying illustrations show the steps in technique.

FROM THE SURGICAL UNIT, CARDIFF ROYAL INFIRMARY

TECHNIQUE OF OSTEOPLASTIC CRANIOTOMY

LAMBERT ROGERS, M.Sc., F.R.C.S., F.A.C.S., F.R.A.C.S., Cardiff, Wales

OSTEOPLASTIC craniotomy is nearly 50 years old for it was on November 23, 1889, that Wagner of Konigshuette first performed the operation of turning down an osteoplastic flap from the skull of a young man unconscious as the result of a head injury. Supratentorial intracranial lesions are now generally approached through an osteoplastic flap and occasionally a similar method of approach is employed for suboccipital lesions also. The advantage of the method is that if a sufficiently large flap is designed, ample access is afforded and its subsequent replacement restores the continuity of the skull completely (Fig. 1). Whenever possible, the flap is designed so that its base lies in the temporal region and hinges on the temporal muscle, then if it is subsequently decided to leave a bone opening for decompression this can be placed beneath the temporal muscle.

INDICATIONS

The operation is undertaken to explore the intracranial contents with the object of carrying out surgical procedures on the cortex, the cerebral vessels, or the choroid plexuses, the removal of, or other treatment of tumors and occasionally also for the drainage, decompression, or removal of abscesses. The operation here described is for an intracranial tumor.

PRELIMINARY VENTRICULOGRAPHY

Many cases require ventriculography for the exact localization of the lesion, and as a rule this is carried out immediately prior to the craniotomy, the site of which is then determined by inspection of the wet x-ray films which are brought to the theater with the return of the patient from the radiographic department. Any risk which ventriculography may involve is appreciably diminished if the craniotomy is proceeded with immediately.

DANGERS AND POSSIBLE COMPLICATIONS

Special equipment is necessary (endothermy apparatus, perforator and burrs, craniotome,[1] hot saline stream, suction, silver clips, etc.) and the employment of a specialized technique which can be but outlined here. It is essential to proceed gently and deliberately, scrupulously guarding the patient against the loss of blood and the tissues from heavy retraction or rough manipulations of any kind. Blood pressure and pulse tracings are made every 5 minutes and recorded on a board for the ready inspection of the operating surgeon so that the condition of the patient is observed and recorded throughout the operation. Rectal saline is given during the operation by a slow drip through a fine rubber catheter. Rigid asepsis is particularly necessary since the operation may last some hours during which the exposed field may easily be contaminated. To touch on only one point of this aspect, the whole theater staff wear non-penetrable masks which include the nose and so deviate the air current from the field in front of them, rather than gauze which even in many layers is a poor filter for arresting organisms.

The dangers of the operation to be avoided are chiefly hemorrhage and rough handling which may lead to shock and an alarming fall in blood pressure. Blood transfusion may be required during the later stages of the removal of a tumor or other lengthy intracranial procedure. After the completion of the operation the chief danger is bleeding beneath the bone flap which may lead to the patient becoming stuporose or comatose from clot compression and necessitates his return to the theater for elevation of the flap and evacuation of the hematoma. Postoperative hyperpyrexia (e.g. 107 degrees F.), particularly liable to arise after operations in the subthalamic region, calls for ventricular tapping and cold sponging.

TECHNIQUE

Preparation of the patient. The case being one of suspect tumor the patient (who has previously been dehydrated by magnesium sulphate (6 drachms per oz.) given 6 hourly by rectal administration for some days beforehand, and who during this time has also had 10 grains of hexamine given thrice daily) has the head completely shaved and the scalp surgically cleansed by wash-

[1]The Gigli wire saw is used in many clinics but in the Surgical Unit at Cardiff we use an electrically driven craniotome, the "skull plough."

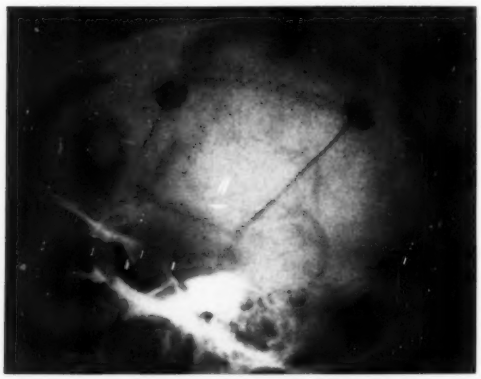

Fig. 1. Bone flap cut by "skull plough," replaced in position after the removal of a Sylvian fissure meningioma. Three silver clips can be seen and some large vascular channels in the bone.

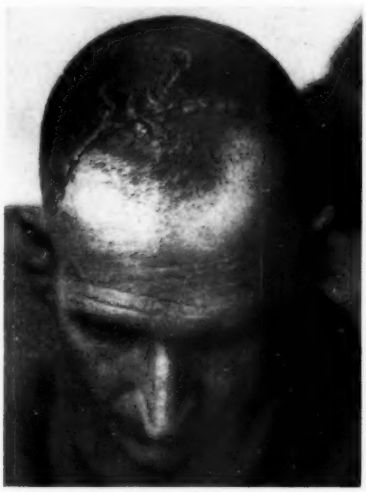

Fig. 2. Scalp incision for approach to the pituitary region. The bone flap was cut with the "skull plough" and a suprasellar cyst, the size of a golf ball, removed.

ing with ether soap and the application of spirit. Ventriculography[1] is then performed and a decision is reached regarding the position of the lesion.

Position of patient and anesthesia. The patient is placed with the head supported on a small circular outrigger and fixed with strapping with the side of the lesion uppermost. Supports and towels are then arranged to shut off the rest of the patient and leave the mouth and nose free. Behind this screen of towels the anesthetist or his assistant records the blood pressure and pulse readings. It is only rarely (e.g., when it is not possible to obtain the collaboration of the patient as may happen in some cases of frontal tumor) that ether or some other form of general anesthetic is required. Local analgesia by procaine (1 per cent) with 5 drops of adrenalin per ounce is used for most cases, the scalp being widely infiltrated with this solution.

The scalp flap. A flap is fashioned so that when turned down there will be an adequate area of the skull from which to fashion the bone flap, and at the same time the scalp incisions are designed so that they lie entirely within the hair line and the forehead is therefore not subsequently scarred. This may necessitate the cutting of a scalp flap which is a good deal larger than the proposed bony one, e.g., in order to cut a frontal bone flap for approaching the hypophysis the incision may need to pass from the top of one pinna almost to that of the other side (Figs. 2, 3, 4). The design of the flap having been decided upon it is cut bloodlessly, the vessels on one side of the incision being controlled by pressure from the surgeon's free hand, those on the other side by the pressure of the hand of an assistant. Small artery forceps are then applied close together to the cut edge of the epicranial aponeurosis (galea aponeurotica) which is everted by them toward the wound edges. The forceps are then collected up into bundles and kept neatly together by means of rubber bands placed round their stems and handles. The incision through the scalp goes right down to the pericranium.

The bone flap. This is cut with the skull plough (Fig. 5), an electrically driven craniotome,[1] after burr holes have been made through which to introduce the dura guard and separator attached to the instrument. It will be seen (Fig. 1) that a minimal number of burr holes is necessary and the base of the flap cracks along a straight line since this terminates in saw cuts.[2] The flap is cracked across the base and reflected outward on its attachment to the temporal muscle.

Any bleeding from the bone flap edges is controlled by pressing warm Horsley's wax into them. In the case of some tumors, e.g., meningiomas, the bone may be extremely vascular because of the presence of large diploic channels (see Fig. 1). Bleeding from these, however, is easily controlled

[1]It is not proposed to describe the technique of this procedure here; methods are similar in most clinics, the vestibules of the lateral ventricles being entered by needles introduced through burr openings at or near Keen's point on either side of the midline in the supra-occipital region.

[1]Brit. J. Surg., 1930, 18: 221.
[2]Nature, November 15, 1930.

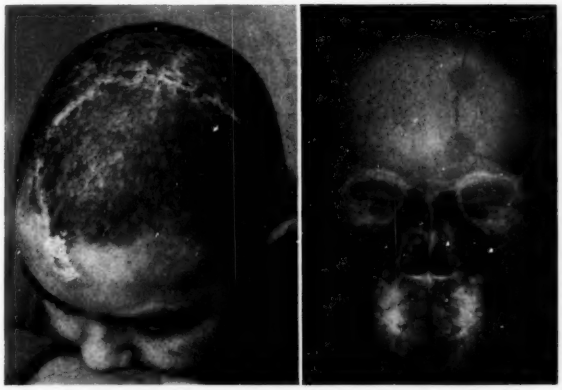

Fig. 3. Scalp incision and position of bone flap cut with "skull plough" for removal of pituitary tumor. In this case the tumor was a chromophobe adenoma.

if the skull plough is used, because as the bone is rapidly divided the saw cut is filled with wax which is pressed into it. If the method employed in some clinics of passing guides and using wire saws is followed, blood loss may be considerable under these circumstances.

Methods of dealing with tumor. The operation of osteoplastic craniotomy which in this sense may be compared with laparotomy is merely the prelude to what may be a lengthy and intricate procedure necessary for the removal of a tumor or for some other purpose which cannot be considered in this article, concerned only with the technique of the flap operation. In the present case, a woman aged 43 years, for 3 years had had frontal headaches, attacks of vomiting, and recently had noticed her sight becoming dim. The optic discs showed choking proceeding to secondary atrophy. There was no muscular weakness. A large space-occupying lesion occupied the right cerebral hemisphere since ventriculography showed that the whole ventricular system was considerably displaced toward the left side of the skull. Through a right osteoplastic supratentorial craniotomy, a Sylvian fissure meningioma was removed after several hours' work with the endothermy apparatus, the use of wet saline cotton wool pledgets, and gentle teasing away and separation of the lesion.

Closure. On the completion of the intracranial operation the bone flap is replaced entire except when a subtemporal decompression is required in which case its base is removed by nibbling forceps. In many cases, particularly pituitary tumors, a small glove drain leading down to the operation field is led out through one of the burr holes at the edge of the flap. This drain is usually removed on the third or fourth day. The cut edges of the dura are drawn against the bone with fine silk sutures to obliterate any space in which clot may subsequently collect and the bone flap is secured in position by perforating its edges at two or three places corresponding to similar perforations made in the surrounding bone. Fine silk sutures are then passed through these openings and tied in position. The scalp flap is then replaced, its surface and the surrounding skin when exposed being at once wiped over with gauze soaked in spirit because of possible contamination from the sweat glands. The epicranial aponeurosis is approxi-

Fig. 4. Lateral view of bone flap shown in Figure 3.

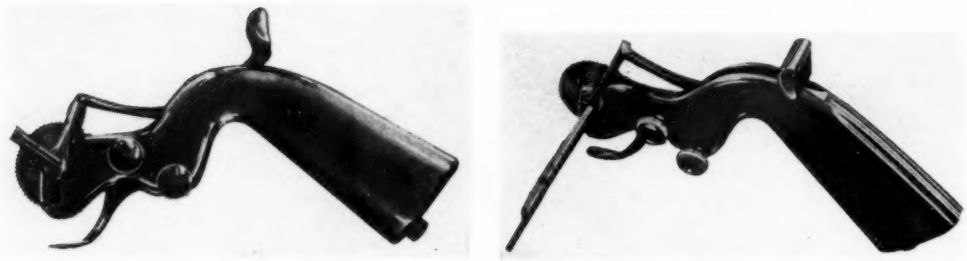

Fig. 5. Side view of "skull plough," at left, and at right, view from above and to the side. (Courtesy Brit. J. Surg., 1930, 18: 221.)

mated with a series of interrupted fine silk sutures and the scalp edges with similar sutures of waxed thread. A dressing of gauze wrung out of spirit is applied and fixed in position with a head (capeline) bandage.

AFTER-TREATMENT

The edema which is liable to follow the intracranial manipulations is checked by continuing the rectal magnesium sulphate administration already referred to, while the fluid intake by mouth is limited. The patient's head is propped up on pillows to lessen venous congestion, and hexamine by mouth is continued. Pulse and temperature are watched, and drowsiness or hyperpyrexia particularly looked for and dealt with in the manner already referred to. The dressing is left undisturbed for 3 days unless bleeding or discharge from drains necessitates its earlier changing or replacing. On the third day it is replaced by a fresh one of sterile gauze. On the fourth day alternate scalp sutures are cut, on the fifth the remainder, on the sixth the first lot are removed, on the seventh the second lot. In this way injury to the suture line is minimized and by the end of a week all sutures have been removed. Dependent upon the condition for which the intracranial operation is performed the rectal magnesium sulphate may be stopped in 4 days' time or continued for a week or longer.

AN OPERATIVE TECHNIQUE FOR THE TREATMENT OF VESICOVAGINAL AND URETEROVAGINAL FISTULAS

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As the result of improved obstetrical methods the incidence of vesicovaginal and ureterovaginal fistulas following parturition has materially decreased. However, these lesions still occur following childbirth and gynecological operations and, when they do, they present just as serious problems in their treatment as was formerly the case. One has but to study the history of the development of the operative procedures used in the treatment of the vesicovaginal fistula, so well presented by Norman Miller, in order to appreciate the difficulties and disappointments accompanying surgical efforts to correct this condition.

The successful repair of vesicovaginal and ureterovaginal fistulas depends upon a number of factors. The choice of an operative procedure should be governed almost entirely by the findings in each case. Kelly, in 1906, reported from the literature 11 different surgical approaches for the cure of vesicovaginal fistulas alone. Of these only 4 are now considered acceptable. It is necessary to remember that these patients should not be operated upon too soon after the injury is sustained. In some cases it is necessary to wait 3 or 4 months before attempting closure. During that time measures to make the future field of operation as healthy as possible should be instituted. These may consist of hot baths, douches, vesical lavage, and urinary antiseptics. Other factors that may prevent the successful repair in these cases are: the presence of poor tissue due to excessive scarring and unsatisfactory blood supply, too much tension on sutures resulting from unsatisfactory mobilization of tissues, infection, and failure to keep the operative site as dry as possible after operation.

A review of the literature on the operative treatment of these lesions as well as the preoperative and postoperative care of patients would seem to indicate that very little that is new could be suggested. In surgery it occasionally happens that some very essential step in surgical technique or in the preparation and care of the patient has been tried and discontinued because of failures that were due to other factors, that either were not recognized or were beyond the surgeon's control at that time. Unfortunately, the true worth of the procedure that was mistakenly discredited may not be appreciated again until long after the factors that actually caused failure have been recognized and corrected. For example, it seemed to us that in view of the fact that we routinely placed our patients on their abdomen following operation, it would be advisable to tie up their bowels to guard against soiling of the wound and to prevent any trauma of the repaired area that might result from straining at stool. Little or no emphasis on the importance of this procedure is found in the more recent articles on this subject, and yet in 1852 we find that its value was stressed by J. Marion Sims. In those patients in whom the vaginal approach seemed indicated it seemed to us that the operation might be made less difficult if an instrument, such as the Freiberg seminal vesical tractor (Fig. 2), were passed through the fistulous vaginal opening to the bladder so that, by traction, the operative field could be brought into better view and a cuff of mucosal tissue could be better dissected by working against the open blades in the bladder.

Inasmuch as we have introduced some modifications in the operation for the repair of the vesicovaginal and ureterovaginal fistulas and have made use of certain procedures in the preparation and care of the patient, which have received little or no recent mention and which we believe contributed materially to the very satisfactory results obtained, we feel justified in reporting the following cases somewhat in detail:

CASE 1. C. S., S. M. H., No. 118474, aged 28. The patient was first seen on November 30, 1936, 12 weeks after the birth of her first child. The labor had been a difficult one, terminated by the application of forceps. The baby was large, weighing 10½ pounds. Practically complete incontinence of urine had been present since that time. Examination revealed a vesicovaginal fistula, nearly 1 centimeter in diameter, which on cystoscopic examination was found to be close to the vesical orifice and adjacent to the sphincter. A roentgenogram of the pelvis showed a widening of the left sacro-iliac joint as well as separation of the symphysis pubis. Both ureters were observed to function satisfactorily and neither was involved in the injury. The condition of the tissues was not satisfactory for repair at

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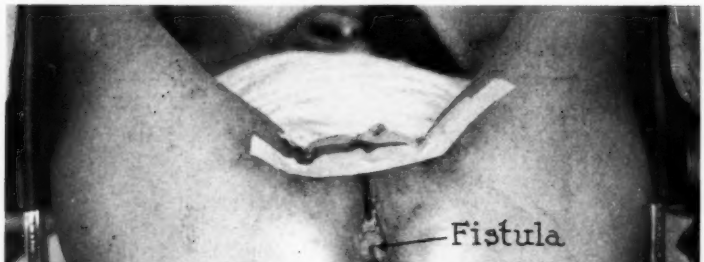


Fig. 1. Patient in position on Young table. Ureteral catheters fixed in place. Note splendid presentation of fistula for vaginal repair operation.

this time, so she was discharged and readmitted 3 months later. During this interval the incontinence of urine persisted and unfortunately she had developed a suicidal complex as a result of it. It was, therefore, of the utmost importance that the operative procedure be followed by a successful result.

In preparation for operation, the bowels were thoroughly cleared, she was given daily bladder irrigations for 4 days prior to operation, and vaginal douches of Dakin's solution twice daily. The day before operation ureteral catheters, No. 7 F., were passed to the kidneys and left *in situ*. As we proposed to keep the patient lying in the prone position for some days after operation, she was kept in this position for several hours each day before operation in order to accustom her to it.

Operation was carried out by vaginal approach. For any such vaginal operation, position of the patient to permit proper exposure is a matter of some importance, though often the position used may be determined by the personal predilections of the operator. Thus the Sims position, the knee chest, the inverted Trendelenburg, and the exaggerated lithotomy positions have been the positions most frequently employed for operation. The exaggerated

Fig. 2. The Freiberg seminal vesical tractor with blades opened and closed.

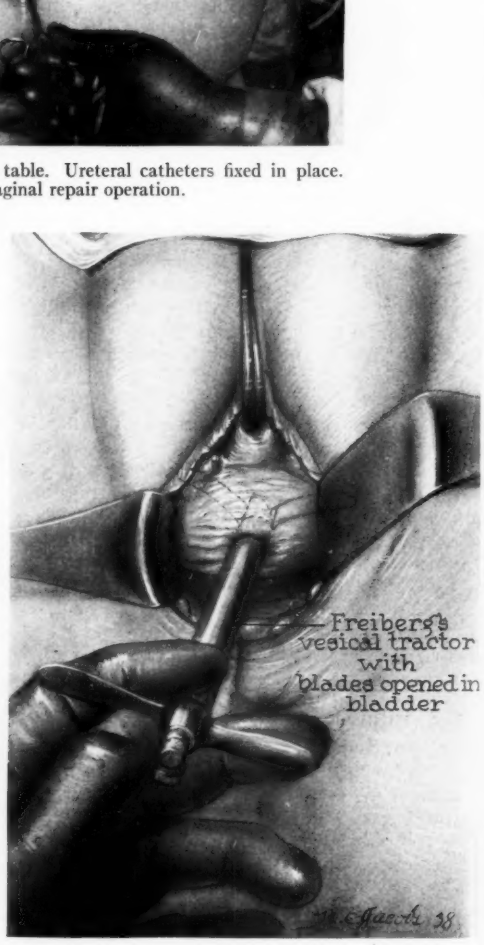


Fig. 3. Freiberg's seminal vesical tractor introduced through opening of fistula and blades opened in bladder.

lithotomy position, as employed by Simon in the 1860's, is infrequently used today, but in our patient it appeared to offer the best exposure. To obtain and maintain this position, we used the Young prostatectomy table with great satisfaction (Fig. 1).

In order to obtain still better exposure, and at the same time to obtain counter pressure while the necessary dissection was carried out, Freiberg's seminal vesical tractor (Fig. 2) was inserted into the fistula, the blades were opened, and moderate traction was made on the handle (Fig. 3). This procedure reverses that suggested by Young for improving the exposure of the operative area in the transvesical approach to vesicovaginal fistula. In this instance it proved to be of great help and undoubtedly made the subsequent steps much easier of execution. An excellent exposure of the fistula was obtained by making moderate traction on this instrument. A circular incision was then made through the vaginal mucosa, approximately 1 centimeter from the margin of the fistulous tract (Fig. 4). By further dissection the fistulous tract was freed from the muscle wall of the bladder down to the bladder mucosa. A pursestring suture of No. 1 chromic catgut was placed in the base of the fistulous tract (Fig. 5, a). After this suture had been placed the blades of the tractor were closed and the instrument removed. The fistula was then inverted and the pursestring suture was firmly tied (Fig. 5, b). By further dissection the vaginal mucosa was freed from the underlying bladder wall until the edges came together easily and without tension, such scar tissue as was present being excised. The edges of the bladder muscular wall were sutured with interrupted No. 1 chromic catgut sutures (Fig. 5, c). After a small amount of redundant vaginal mucosa had been excised the vaginal wound was closed by a continuous No. 1 chromic catgut suture, this suture line being at right angles to the underlying suture line in the bladder wall (Fig. 6, a and b). This step completed the operation.

In order to keep the operative site just as dry as possible, the ureteral catheters which had been passed the day before

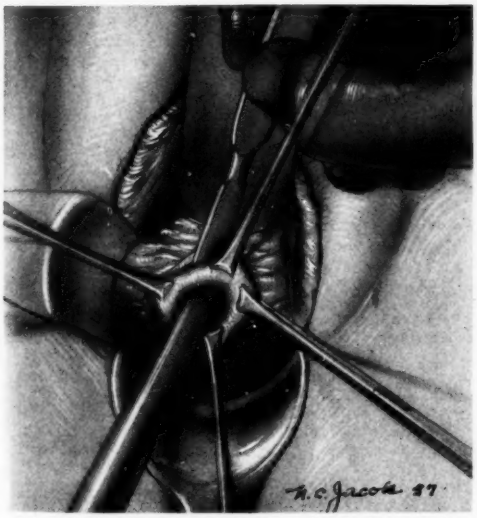
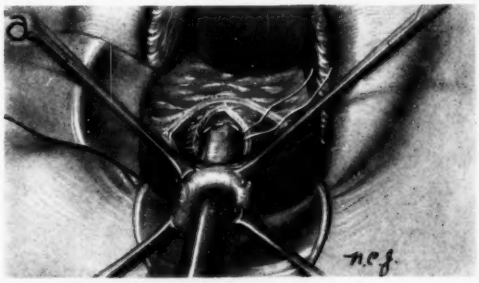


Fig. 4. The dissection of the mucosal cuff of the fistulous tract. Traction being made by the seminal vesical tractor.



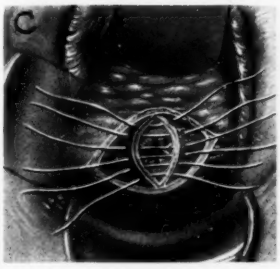


Fig. 5. a, The mucosal cuff dissected and pursestring suture placed. b, Inversion of cuff. c, Interrupted catgut sutures placed for approximating edges of bladder.

operation were left *in situ;* and to provide drainage for such urine as might leak into the bladder around these, a No. 18 F. urethral catheter was passed and all 3 held in position by silk sutures.

The patient was placed in the prone position, and this was maintained for 12 days. In order to prevent undue physical effort, and also the possibility of soiling of the operative site, she was placed on liquid diet and the bowels were not allowed to move during the time she was kept in the prone position. It had been planned to leave the ureteral catheters in place for 6 days, but the left one became blocked on the fifth day and was removed; the right one was removed the following day. The urethral catheter was left in the bladder during the time the prone position was maintained. Urinary antiseptics were administered during this time.

The convalescence was entirely satisfactory and perfect healing of the operative site resulted with complete urinary control.

CASE 2. E. D., S. M. H., No. 134530, aged 50. This patient developed a large vesicovaginal fistula following cauterization of the cervix and the repair of a cystocele. Four months later, on April 27, 1938, she entered the hospital for operation. On examination a large fistula was

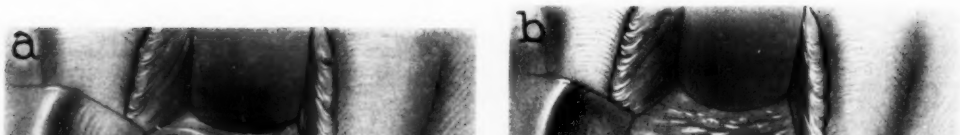


Fig. 6. a, Closure of bladder wall. b, Approximation of mucosal surfaces of vagina.

found posterior to the vesical orifice and slightly to the left of the midline. The patient was treated in a manner identical to that described in the previous case with equally satisfactory results.

CASE 3. S. D., S. M. H., No. 129920, aged 47. In April, 1937, the patient was operated upon elsewhere for fibroids of the uterus. The ovaries, tubes, and uterus, including the cervix, were removed. She reported that she was severely ill immediately following her operation and for several weeks afterward. Three days after the operation she began to drain all of her urine through the vagina.

She was first seen in the clinic on July 14, 1937. Aside from moderate cardiac enlargement and a systolic murmur her physical findings were essentially normal except for the bladder and vagina. The vaginal mucosa was red and inflamed; and in the vault, on the anterior wall, and rather far to the right of the midline was a small patch which we assumed at that time to be granulation tissue. About 3 centimeters below this point and a little to the right of the midline was the opening of a vesicovaginal fistula about 1.5 centimeters in its greatest diameter. On cystoscopic examination a vesical calculus 1.5 centimeters by 1 centimeter was found and removed. It was difficult to distend the bladder because of the fistula. The bladder mucosa was markedly inflamed and congested. The left ureter was easily catheterized. The opening of the vesicovaginal fistula was located about 2 centimeters above the level of the right ureter. Attempts to catheterize the right ureter were unsuccessful and at that time it was thought our difficulty was due to a stricture or a sharp angulation of the ureter due to trauma. The patient was discharged on a routine of urinary antiseptics, douches, and bladder irrigations in preparation for a repair operation.

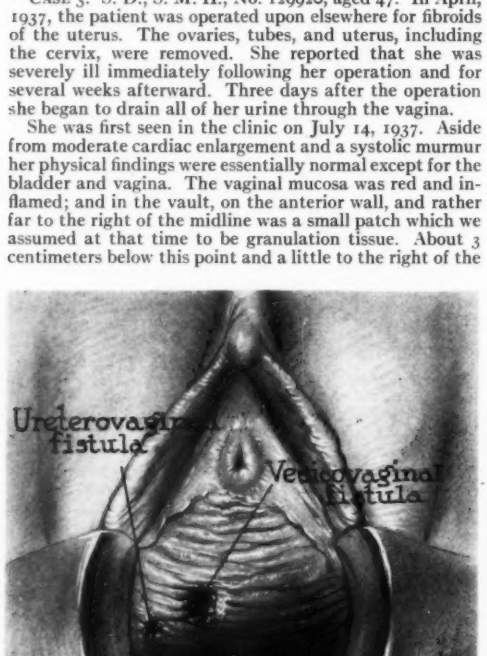


Fig. 7. Vaginal presentation of vesicovaginal and ureterovaginal fistulas.

The patient was next admitted to the hospital in a critical condition due to acute rheumatic fever on October 28, 1937. Her course in the hospital was very stormy and she was not discharged until January 4, 1938. Her diagnosis at that time was acute rheumatic fever with carditis and myocarditis, pulmonary stenosis, mitral stenosis and insufficiency, interventricular conduction defect with left bundle branch block, and ventricular extrasystoles.

On July 26, 1938, she again entered the hospital. The condition of the tissue of the vagina and bladder was markedly improved and it was found that the tuft of red tissue in the vagina, previously assumed to be granulation tissue, represented the vaginal orifice of a ureterovaginal fistula (Fig. 7). The patient's cardiac condition was still far from satisfactory; there was marked dyspnea, the pulse was fast, and her basal metabolism reading was plus 41.

The suprapubic approach was selected for a number of reasons. The vesicovaginal fistula was located high in the vault of the vagina. From the location of the orifice of the ureterovaginal fistula in the vagina it appeared as though the remaining portion of the ureter would be too short to permit sufficient mobilization for transplanting it to the bladder through the vaginal route. Furthermore we were informed by our medical confrère that the patient's dyspnea was such that it would be impossible to lower her head sufficiently for the vaginal operative approach. On account of the dyspnea cyclopropane anesthesia was used.

Suprapubic repair of vesicovaginal and ureterovaginal fistulas with transplantation of the right ureter to the bladder was performed. The right ureter was catheterized through the vagina where it opened into the latter and the catheter was fixed in place as an aid in locating the lower end of the ureter from above. The patient was placed in the usual position for the suprapubic transvesical approach to the bladder except, for the reasons stated, the head was

not lowered. A midline incision was made and the bladder was exposed and opened. Although it was a little difficult because of the patient's position and the previous operation with its subsequent infection, the peritoneum was separated from the bladder and held out of the way by packs. The lower end of the right ureter was mobilized sufficiently to reimplant in the bladder without too much tension and then freed from the vagina at its point of attachment, and the ureteral catheter was drawn out from below. The vaginal opening was closed from above with interrupted No. 1 chromic catgut sutures, care being observed to invert and approximate the vaginal mucosal surfaces. The line of cleavage between the vagina and bladder was easily developed, the vesicovaginal fistula was isolated and cut across, and the dissection carried well below its point of attachment to insure full mobilization of the vagina and the base of the bladder. The mucosal surfaces of the vaginal wall were inverted into the vagina and the opening was closed by interrupted No. 1 chromic catgut sutures. The mucosal surfaces of the bladder portion of the fistula were inverted into the bladder and approximated by a continuous suture of No. 00 chromic catgut. The musculature of the bladder was closed by interrupted sutures of No. 2 chromic catgut placed at right angles to those inserted in the vagina. As a result of placing the sutures as described and the liberal mobilization of the bladder and vaginal walls, the repaired areas in both organs were no longer in contact with each other. A No. 7 F. ureteral catheter was then passed up the right ureter to the kidney and the very tip of the severed ureter was tied firmly to the catheter. A small stab wound was made in the posterior wall of the bladder at a point where the ureter could be implanted with the least tension, and the catheter and the ureter were drawn through the opening into the bladder. After the reimplanted ureter was fixed to the bladder by 3 No. 00 chromic catgut sutures the ligature attaching the ureteral wall to the catheter was cut. A No. 7 F. ureteral catheter was passed to the left kidney pelvis and the ends of both catheters were passed through the urethra and fastened in place with silk sutures. The bladder was closed about a mushroom catheter placed suprapubically, and the space of Retzius was drained by a small tube and a cigarette drain. The customary closure for wounds of this character was made. The patient's condition was fair at the end of operation.

Upon return to the ward the patient was placed on her bdomen on a Bradford frame to facilitate drainage and prevent the puddling of any urine that might drain around the ureteral catheters. The same postoperative routine previously described in the care of Case 1 was followed. The ureteral catheters were removed in 7 days and in 21 days she was removed from the Bradford frame and placed on her back. The small suprapubic catheter that was draining the bladder at this time was removed and a small urethral catheter was placed to hasten healing. The suprapubic wound re-opened once following the removal of the urethral catheter. The patient's convalescence was slow because of her very poor general condition. Five weeks after operation she suffered a severe attack of rheumatic fever with marked accentuation of her cardiac symptoms and enlargement of her joints, the right knee joint being especially involved. It was 4 weeks before she had recovered sufficiently from this attack to be discharged from the hospital. The implanted ureter was dilated 12 weeks after operation and a normal pyelogram was obtained. The vesicovaginal fistula healed *per primam*. A retrograde study of the right kidney and ureter was made 13 months after operation and they were found to be normal.

SUMMARY AND CONCLUSIONS

The successful pre-operative and postoperative routine as well as operative technique employed in the repair of vesicovaginal and ureterovaginal fistulas is presented.

In no surgical condition will the meticulous attention to detail, the operative technique, and the pre-operative and postoperative care of the patient pay greater dividends in the way of good results than in the treatment of vesicovaginal and ureterovaginal fistulas. This small group of cases is presented to emphasize this point, and while the technique presented suggests no marked fundamental changes we believe that the accessory procedures employed during and after the operative care of these patients did contribute materially to the satisfactory results obtained.

We would emphasize the value of the special tractor in facilitating the necessary dissection. This instrument in its present form could be used only in the case of the large fistula, but a modification of it could be adopted to those of a much smaller size. Keeping the operative site just as dry as possible is of the greatest importance during the healing process. The prone position facilitates this as does also the use of ureteral catheters in addition to the usual in-lying urethral catheter. These may be left *in situ* for as long as 8 to 10 days if it seems desirable. In using ureteral catheters every effort should be made to prevent renal infection. Oral urinary antiseptics should be started as soon as possible after operation.

Keeping the patient on a slight residue diet and preventing evacuation of the bowels for 10 to 12 days, reduces the handling of the patient which would otherwise be necessary, and also reduces the possibility of the contamination of the operative site. The operator should be guided in his choice of procedure by the finding in each case. The patient should be instructed to refrain from sexual intercourse for at least 3 months after operation.

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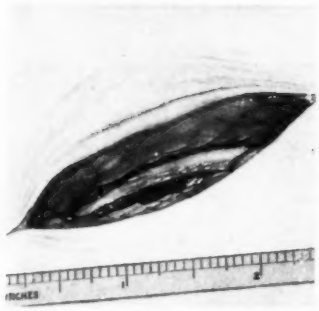

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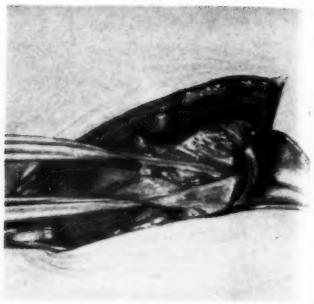

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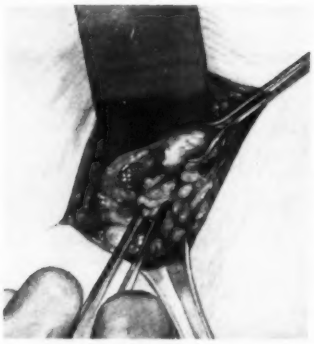

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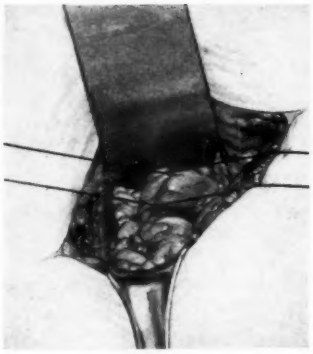

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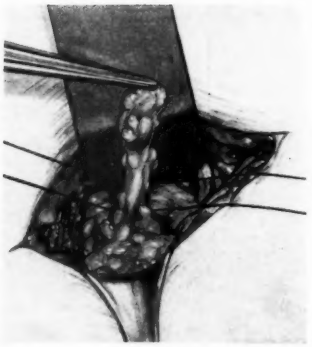

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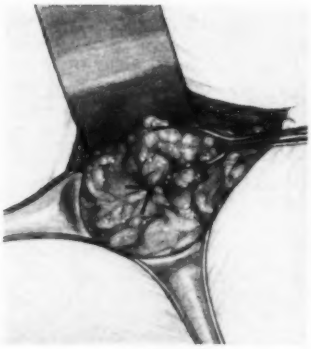

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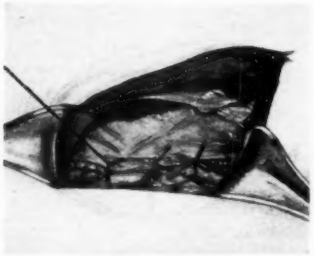

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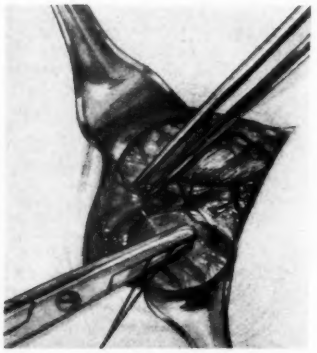

Fig. 9.

Fig. 1. The skin incision 2½ to 3 inches long, made transversely in the general direction of the fibers of the transversalis.

Fig. 2. Median half of anterior rectus fascia cut across.

Fig. 3. The right rectus muscle is pulled laterally and the fibers of the transversalis muscle are exposed. Here they are thinned out as a fascial plane and fused with the peritoneum. This layer was incised transversely in direction of the fibers and the margins grasped with hemostats.

Fig. 4. The duodenum has been picked up with a Babcock forcep and retracted to the left. The liver is held up with a Deaver retractor. The thumb forcep is grasping a tag of the gastrocolic omentum.

(*Balance of legends on opposite page.*)

Acute Perforated Peptic Ulcer; Simple Closure Through a Short Transverse Incision.—
John B. Hartzell and Milton L. Sorock.

ACUTE PERFORATED PEPTIC ULCER

Simple Closure through a Short Transverse Incision

JOHN B HARTZELL, M.D., F.A.C.S., and MILTON L. SOROCK, M.D., Detroit, Michigan

THERE has been a recent revival of interest in the advantages offered in the use of the transverse type of incision in abdominal surgery. In general, the transverse incision possesses the definite anatomical advantage in preserving the nerve and blood supply of the abdominal muscles. There is another important factor which is frequently overlooked, namely the preservation of the fibers of the transversalis and internal oblique muscles, which are severed in the vertical incision. This point has been stressed by Quain, Sloan, Batson, Singleton, Hartzell and Winfield, and also recognized by Clute, Pool, Lynn, Meleney and Howes, and others.

The simplified approach to ruptured gastric and duodenal ulcers through the small oblique incision, as described by Amendola, appeared to have decided merit. During the past year, we have used this incision in a slightly modified form in 39 cases.

We make our incision more horizontally than does Amendola, starting in the midline about 2 inches below the costal border (if possible, always at, or just below the liver border, and extending 2½ to 3 inches to the right). The incision is carried through the skin, subcutaneous tissue and the anterior fascia of the rectus muscle. The muscle is then freed from its sheath for a short distance and retracted laterally. The fibers of the transversus abdominus muscle and the peritoneum are split transversely, a finger is inserted, and usually the ulcer is easily palpated. Most frequently it is felt to the right of the incision. If the liver is low, it may be elevated out of the way with a Deaver retractor. The duodenum is grasped with a Babcock forcep and retracted to the left. If the operator now stands on the patient's left side, he will usually look directly downward upon the perforation, which is easily closed, as shown in the illustration. Rarely this incision does not afford adequate exposure, and the fibers of the rectus muscle may then be cut across, and the incision extended transversely as far as the lateral border of the rectus muscle. This procedure will usually afford adequate exposure in even the most difficult cases. Although on several occasions this small incision has been extended upward from the inner angle, downward from the outer angle, while on one occasion, where the ulcer was high on the gastric wall, it was extended across the midline an equal distance, and the left rectus muscle was retracted laterally.

During the past 6 years, there have been 273 patients with acute ruptured ulcer of the stomach and duodenum operated upon at the Receiving Hospital, with 73 deaths. Two hundred and thirty-four of these were operated through vertical right rectus incisions, with a mortality of 28.9 per cent. In this group of cases, there were 6 wound disruptions with evisceration, an incidence of 2.6 per cent. Three of these died. During the past year 39 ruptured ulcers have been repaired through the transverse incision, with 5 deaths, a mortality of 12.8 per cent.

We do not wish to emphasize the lower mortality in the group operated upon through the

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Fig. 5. The ulcer is closed by simple inversion. We do not hesitate to use the Graham method of closure in those cases in which a friable indurated area about the ulcer does not permit of simple inversion.

Fig. 6. A tag of omentum is tied with the same sutures. When such a tag is not available, we sometimes split a graft from the ligamentum teres, or use a free omental graft, as described by Graham.

Fig. 7. Omental tag is tied in place over closed ulcer.

Fig. 8. The transversalis fascia and peritoneum (posterior rectus sheath) are closed as one layer.

Fig. 9. When lateral traction on the muscle is released, the medial border returns to the midline, and the anterior rectus fascia is closed.

Fig. 10. The skin margins are approximated.

Figs. 11 and 12. Healed cases 1 to 2 weeks after operation.

transverse incision, as to date we have not had a sufficiently large group of cases. We believe, however, that this simplified method of approach has many advantages. It is easy to accomplish in the majority of cases. We have been able to operate in several cases in which patients were practically *in extremis*, using local novocain injections where no attempt was made to obtain relaxation.

Quite a number of the patients develop severe wound infections, and when the small incision is used, even when disruption takes place, evisceration or incisional hernia has not occurred. The small bowel is not visualized, and consequently is not traumatized by being held out of the way in order to obtain exposure. The wound is more easily closed even in the absence of relaxation. The patient is far more comfortable and is able to move about in bed with little difficulty. The morbidity is shortened, the patient is out of bed sooner, usually the seventh to the eighth day and, therefore, is discharged from the hospital at a correspondingly earlier date.

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PROBLEMS IN DIFFERENTIAL DIAGNOSIS BETWEEN UROLOGIC AND ABDOMINAL LESIONS

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IT is hardly necessary at this time to emphasize the importance and value of making an accurate pre-operative diagnosis. Such a diagnosis enables the surgeon to plan the operative procedure; the technical steps of the operation can be carried out rapidly and, as a result, complications are relatively rare and the morbidity is greatly reduced.

Activities of the urologist are no longer limited to the realm of diagnosis and differential diagnosis of lesions of the genito-urinary tract, since he is called upon with increased frequency to aid in solving problems of differential diagnosis between lesions of various abdominal organs and the genito-urinary organs. Furthermore, he is called upon more frequently than formerly to solve differential diagnostic problems in the field of general diagnosis.

The urologist is confronted not only with pre-operative problems of differential diagnosis between abdominal lesions and lesions of the genito-urinary tract, but he is frequently called upon after operation. He must be familiar, therefore, with the various urological complications following general surgical as well as gynecological operations.

From the urologist's point of view the problem of differential diagnosis is concerned with (1) a consideration of the various intra-abdominal and retroperitoneal lesions that may be confused with urological lesions; (2) with postoperative complications in the urinary tract; (3) with complications arising from the pathological process for which the patient was operated upon, these complications being confused with lesions in the urinary tract; and (4) with lesions that are not recognized until after the complications arise and which demand consideration in order to determine the cause of the patient's condition after operation.

Before entering into a detailed discussion of some of these problems, it might be desirable to emphasize that here, as in any problem of diagnosis, great care must be exercised in obtaining the history, because from this source one very often gains valuable information that may lead to a correct solution of the problem. Only too frequently errors in diagnosis are made because not enough time is devoted to obtaining the history or because a faulty interpretation is given to the patient's story.

Presented before the Clinical Congress of the American College of Surgeons, New York, October 21, 1938.

LESIONS OF THE GASTRO-INTESTINAL TRACT

Lesions of the gastro-intestinal tract probably constitute the largest group that calls for differentiation and, of these, appendicitis heads the list. The differentiation between lesions of the urinary tract and lesions of the appendix should be relatively simple; however, the large number of patients seen by the urologist each year for the relief of urinary symptoms, in whom an appendectomy has failed to effect a cure, is evidence that the differentiation is not made as frequently as it should be.

At times the differentiation between acute appendicitis and acute pyelitis is difficult, especially if a patient with an acute disease of the appendix has some red blood cells and perhaps a few pus cells in the urine and it is difficult to obtain an accurate history. In a child having acute, severe pyelitis with right-sided pain and tenderness, the differentiation is especially difficult if the urinary findings are negative, as they may be during the first 24 or 36 hours; after the urine becomes loaded with pus, the diagnosis is self-evident. The number of cases in which this differentiation is impossible and in whom it is necessary to perform an appendectomy is very small indeed.

This differentiation may present great difficulties in an adult female who has had severe attacks of pyelitis during one or more pregnancies. If a woman who has previously had attacks of pyelitis suddenly develops an attack of acute appendicitis, it is easy to understand why the attack of appendicitis may be overlooked and the clinical picture attributed to a lighting up of an old infection in the kidney. In this type of case, if after due deliberation and consultation, it is not possible to make the differentiation, one should give the patient the benefit of the doubt and operate on her rather than run the danger of overlooking an acute appendix and having the patient die of generalized peritonitis. The number

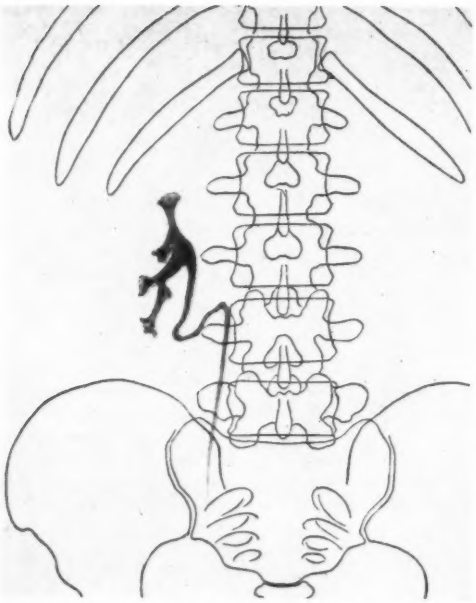

Fig. 1. Case 1. Kink in right ureter. Note absence of hydronephrosis.

of patients in whom this differential diagnostic problem arises, or in whom an appendectomy is performed and in whom urinary symptoms persist, constitutes a relatively small group of cases.

I now wish to call attention to a group of patients in whom no acute problem in differential diagnosis is present. I refer to the large number of patients who are operated upon for appendicitis —generally "chronic" cases in which the patients' symptoms persist after the appendix has been removed. Inasmuch as no acute problem is present, so that no acute surgical emergency exists, it would appear that there would be ample time to establish a correct diagnosis rather than subject the patient to an operation that does not remove the cause of the symptoms. Here again, a careful history and physical examination, coupled with a careful urinary examination, would often lead to a correct diagnosis. In all doubtful borderline cases the patient should have the benefit of a complete urological survey before his so called chronic appendix is removed.

The number of patients who consult the urologist each year for the persistence of urinary symptoms after an appendectomy is legion, and we should make every possible effort to establish a correct diagnosis before operation and thereby institute not only the correct treatment, but avoid an unnecessary operation. The differentiation between lesions of the appendix and of the urinary tract cannot be overemphasized.

Among the more frequent lesions in the urinary tract that are overlooked or confused with chronic appendicitis may be mentioned: chronic pyelitis, hydronephrosis, with or without infection; renal and ureteral calculi; and renal tuberculosis. Among the rare lesions in the urinary tract in which the underlying pathology is not recognized may be mentioned: ectopia of the kidney, solitary fused kidney, and congenital polycystic disease.

At rare intervals confusion arises in the differential diagnosis between lesions of the genital tract in the male, such as seminal vesiculitis, and appendicitis. However, a careful review of the history is of great value as the history in acute appendicitis is quite different from that in lesions of the male genital tract. The rectal examination is most important as it gives information that generally aids in making a differential diagnosis.

LESIONS OF THE GALL BLADDER

The problem of differential diagnosis between lesions of the gall bladder and the kidney, has become greatly simplified since the advent of pyelography and cholecystography. Before the advent of cholecystography the urologist was frequently called upon to aid in differential diagnosis in order to rule out lesions of the kidney in borderline cases. With the advent of cholecystography another important diagnostic aid has been placed at our command, thus leading to more accurate diagnoses of lesions in the right upper quadrant. In a good many cases of right upper quadrant pain pyelography or cholecystography will suffice.

There remains, however, a small group of cases in which the patient has a lesion both of the kidney and of the gall bladder, so that at times it is difficult to state whether the symptoms of which the patient complains are due to one lesion or to both. A good deal of study may be necessary in order to determine which of the two lesions is responsible for the patient's symptoms so that the correct surgical procedure may be instituted:

Two cases under recent observation will serve as illustrations:

Case 1. (a) Acute recurring pyelitis; (b) nephroptosis; (c) cholelithiasis. Mrs. F. S., aged 38, was admitted to the Presbyterian Hospital on October 25, 1933. The previous history was irrelevant. The patient complained of pain in the right side, dysuria, difficulty on urination, nausea, vomiting, and weakness. Seven weeks before admission to the hospital the patient was suddenly seized with an acute pain in the right upper quadrant which radiated downward

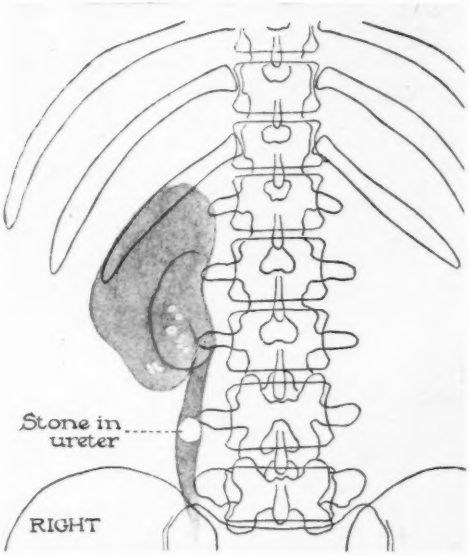

Fig. 2. Case 2. Presence of stone in the ureter, stones in the gall bladder, and the lower pole of the kidney.

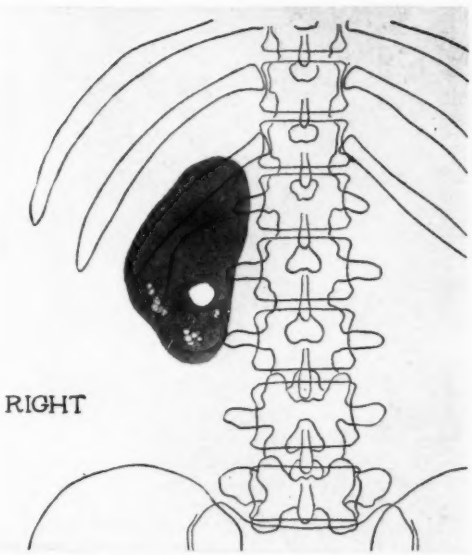

Fig. 3. Case 2. Retrograde movement of stone from the ureter into kidney pelvis. Gall and kidney stones present.

and forward as well as to the back. The pain was associated with nausea and vomiting. The pain subsided, but since then there had been a persistent, dull, steady ache in the same area but of lesser degree. A cystoscopic examination was made elsewhere and a diagnosis of infection of the right kidney was made.

Examination of the head, the neck, the heart, and lungs was negative; examination of the abdomen revealed tenderness over the entire right side. The blood pressure was systolic 126 and diastolic 82.

Blood count showed 4,990,000 red blood cells, 7,200 white blood cells, and a hemoglobin of 95 per cent. Examination of the urine on admission showed no albumin, blood, or pus. A mixed phenolsulfonphthalein showed an output of 59 per cent in 1 hour. Blood chemistry examination: urea nitrogen, 11.8; uric acid, 3.6; creatinin, 1.4; non-protein-nitrogen, 28.8.

Cystoscopic examination revealed a normal bladder and ureteral orifices. The ureters were catheterized without difficulty or obstruction. The urines obtained from the right and left kidneys and bladder were free of pus. The urine from the right kidney was sterile on culture and urine from the left kidney showed 3 colonies of hemolytic Bacillus coli. Culture of the bladder urine showed hemolytic Bacillus coli and Shigella.

Roentgenographic examination was negative for stone in the urinary tract. Shadows were seen that were compatible with multiple stones in the gall bladder. A set of intravenous pyelograms were made and they were normal except that there was a kink in the right ureter (Fig. 1). A cholecystogram showed a poorly functioning gall bladder. The patient was discharged on November 1, 1933.

In view of the fact that the patient has had many attacks of pain in the right upper quadrant, that pus and colon bacilli have been found in the urine from the right kidney at various times, the presence of a normal pyelogram associated with a movable kidney with a kink in the ureter, x-ray evidence of gall stones, and a poorly functioning gall bladder, all led to the conclusion that the cholelithiasis was the primary underlying cause of her trouble, that the infection in the right kidney was secondary, and that operation should be performed on her gall bladder and not the kidney.

Case 2. (a) Nephrolithiasis, right; (b) ureterolithiasis, left; (c) cholelithiasis. Mrs. G. W., aged 33 years, was admitted to the Presbyterian Hospital on November 13, 1938.

A right ureterotomy and a lithotomy were performed elsewhere in March, 1937. The present illness began in August, 1938, at which time the patient had a very severe attack of pain in the right lumbar area. There were nausea and vomiting. The pain gradually subsided and completely disappeared at the end of the fourth day. During this attack the patient had no jaundice, hematuria, or dysuria. On November 2 she had another attack of pain in the right upper quadrant. The patient consulted a physician and a roentgenogram was taken. She was told that she had a stone in the right kidney. The third and present attack of pain began on November 13, 1938. The pain was sudden, sharp, and knife-like and began in the right flank and radiated towards the right upper quadrant of the abdomen. Nausea and vomiting were associated with the pain.

Physical examination revealed temperature, 100 degrees; pulse, 88; respiration, 24. Examination of the head,

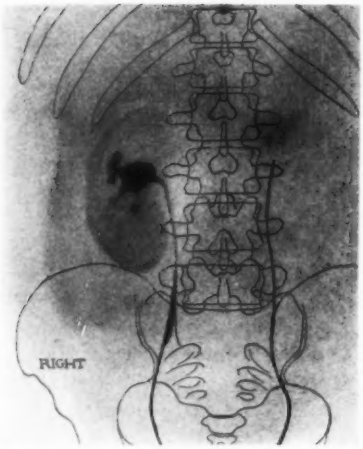

Fig. 4. Case 3. Case of subphrenic abscess. Displacement of kidney and liver downward.

neck, and lungs was negative. A coarse systolic murmur was heard at the apex of the heart. Examination of the abdomen revealed acute costovertebral tenderness posteriorly, and marked rigidity below the costal arch on the right side in the region of the gall bladder.

The urine on admission was normal. Examination of the blood showed 23,400 leucocytes. The phenolsulfonphthalein test showed an output of 50 per cent in 90 minutes.

Roentgenographic examination showed a shadow in the right ureter and 4 small shadows compatible with stones in the inferior pole of the right kidney and a small collection of shadows compatible with stones in the gall bladder (Fig. 2). A cholecystogram demonstrated the presence of stones in the gall bladder. A second film showed the stone, that was previously noted in the right ureter, in the kidney pelvis—retrograde movement of stone (Fig. 3). There were several small shadows compatible with stones in the lower left ureter.

During the period of observation in the hospital the patient passed several small stones corresponding with the shadows seen in the lower left ureter. After the patient had been admitted to the ward it was difficult to interpret the clinical picture. The history of a previous ureterotomy for stone, coupled with tenderness in the right costovertebral angle and pain in the back, justified the diagnosis of renal colic due to stone. The marked tenderness and rigidity over the gall-bladder area justified the diagnosis of a lesion of the gall bladder. After due deliberation a tentative diagnosis of both renal colic and gall-stone colic was made. This was verified by roentgenographic studies.

The sudden relief of the symptoms due to the kidney can be explained by the retrograde movement of the stone from the right ureter into the kidney pelvis, a phenomenon described previously.[1] After this occurred the clinical picture was that of cholelithiasis and operation was advised. A cholecystectomy was performed by Dr. V. C. David on November 23, 1938. The patient made an uneventful recovery and was discharged on December 7, 1938. The patient was readmitted to the hospital on January 6, 1939, and the stone was removed from the kidney on January 10, 1939. The patient was discharged on March 22, 1939.

[1]Kretschmer, Herman L. Retrograde movement of stone in the ureter. J. Am. M. Ass., 1918, 71: 1355.

SUBPHRENIC ABSCESS FOLLOWING PREGNANCY

Although the occurrence of chills and fever, the presence of pain in the right kidney area, and pus in the urine occurring during pregnancy would seem to justify the diagnosis of pyelitis of pregnancy, one must always be on the alert for the possibility of some lesion outside the urinary tract that may be responsible for the clinical picture that may occur during pregnancy or the puerperium. As an example of a case that presented an interesting problem in differential diagnosis, I should like to present the following:

Case 3. (a) Subphrenic abscess; (b) pleural effusion; (c) pyelitis of pregnancy; (d) secondary anemia. Mrs. B., aged 23, was referred by Dr. W. C. Hoyt and admitted to the Presbyterian Hospital on October 23, 1928, with a diagnosis of pyelitis of pregnancy.

Three weeks before admission to the hospital the patient was in her eighth month of pregnancy when she began to develop convulsions and lost consciousness. She was immediately delivered of the child. The child lived 12 hours. Eleven days before she was admitted to the hospital she developed severe pain in the right upper quadrant which was aggravated by breathing. At this time the patient developed severe chills and a temperature of 104 degrees. There was some frequency and burning on urination. The examination of the urine showed the presence of a large amount of pus.

The tongue was dry; pulse, 120; temperature, 102.6 degrees; examination of the heart, negative. The right chest was flat and the breath sounds were distant. The left chest was normal. Examination of the abdomen showed the right kidney enlarged and tender. The lower edge of the liver was 1 inch below the costal arch; the spleen was not felt; the pelvic examination was negative.

Examination of the urine revealed albumen 2 plus, blood 3 plus, and a leucocyte count of 3,200 pus cells per cubic millimeter. Examination of the blood showed 2,660,000 red blood cells, 22,800 leucocytes, and a hemoglobin of 55 per cent. The blood pressure was 160/91. The Wassermann test was negative, and guinea pig tests were negative for tuberculosis.

Cystoscopic examination. Cystoscopy showed a normal bladder and the ureters were catheterized without difficulty or obstruction. Cell count showed 475 white blood cells per cubic millimeter and culture showed Bacillus coli communis in the bladder urine. The urine from the right kidney was free of pus and culture showed Bacillus coli communis. The left side showed 390 white blood cells per cubic millimeter and Bacillus coli communis.

Roentgenographic examination was negative for stone. The right pyelogram showed the kidney pelvis opposite the third lumbar slightly dilated with slight dilatation of the right ureter (Fig. 4). The left pyelogram was normal. Roentgenographic examination of the chest verified the clinical findings of right pleural effusion, made by Dr. E. E. Irons, who aspirated 900 cubic centimeters of turbid fluid. Examination of the fluid aspirated from the chest showed no organisms on Gram stain and no tubercle bacilli were found.

This patient presented a very unusual and interesting problem in differential diagnosis. The history of chills and fever, swelling in the region of the right kidney, and the

presence of pus in the urine, led to the diagnosis of right-sided pyelitis of pregnancy. However, the low position of the liver, and the presence of pus in the left kidney, whereas the right was free of pus, and the low position of the right kidney and the presence of fluid in the right pleural cavity, led to the conclusion that the patient suffered from more than a pyelitis of pregnancy.

The patient was seen in consultation by Dr. E. E. Irons and Dr. V. C. David, and after careful consideration a diagnosis of subphrenic abscess was made and operation advised. The patient was operated upon by Dr. V. C. David on November 3, 1928, and a subphrenic abscess was drained. Examination of the pus from the subphrenic abscess showed gram-positive cocci in groups, a few short chains, and slender gram-positive rods. The patient made an uneventful recovery and was discharged on December 11, 1928.

CYST OF THE PANCREAS

As a general premise one may state that cysts of the pancreas are rare and present no pathognomonic symptoms. Physical examination reveals an elastic swelling in the epigastrium, generally in the midline. The onset is slow and the nature of the disease is progressive. In the majority of cases the swelling comes forward so that it is readily palpable. Displacement of viscera may occur and, in rare instances, there may be displacement of the kidney. Cysts of the pancreas may be confused with lesions of the kidney, such as hydronephrosis and tumor, especially when there is some displacement of the kidney.

Urological diagnostic procedures are necessary to establish the differential diagnosis. In some instances there may be hydronephrosis of a moderate degree due to pressure and, in other instances displacement of the ureter, the kidney, or both may occur. In one of our cases the pyelogram showed that the pelvis of the kidney was normal, and there was displacement so that it formed an obtuse angle with the ureter. As an example of a case in which it was necessary to differentiate between a lesion of the kidney and the pancreas, I should like to present the following case:

CASE 4. (a) Cyst of the pancreas. Mrs. R. H., aged 23, was referred by Dr. I. Rabens.

The previous history was negative. The patient was a bit indefinite about the onset of her symptoms. Her chief complaint was the presence of a feeling of fullness in the upper abdomen. She had suffered from constipation for many years, which was always worse a few days before and after menstruation. Menstruation was generally associated with cramp-like pain in the abdomen. In addition, the patient gave a history of dizziness, pains in the head, and nervousness.

Examination of head, neck, heart, and lungs was negative. Examination of the abdomen revealed a mass in the right upper quadrant. The surface was smooth and the lower pole was at the left of the umbilicus. The lower pole was rounded and the mass had distinct respiratory mobility

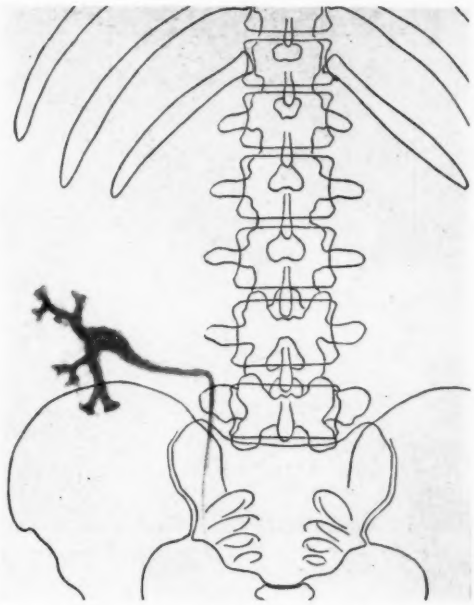

Fig. 5. Case 4. Cyst of the pancreas. Note displacement of renal pelvis and upper ureter.

and seemed to disappear beneath the costal arch. Examinations of the pelvis and central nervous system were negative.

The blood pressure was sytolic 124, diastolic 70. The Wassermann test was negative, and a blood examination showed a slight anemia. The cystoscopic examination was negative.

Roentgenographic examination showed that the left pyelogram was normal. The right pyelogram revealed that the pelvis was normal in size, but that it formed an obtuse angle with the ureter, and there was displacement of the upper portion of the right ureter (Fig. 5).

From the urological findings the presence of a hydronephrosis was excluded and a pre-operative diagnosis of pancreatic cyst was made. An operation was performed and the diagnosis was verified. The patient made an uneventful recovery and was discharged on December 5, 1935.

LESIONS OF THE COLON

Lesions of the large bowel are of interest to the urologist because some of them may result in the production of enterovesical fistulæ. The two lesions most frequently responsible for the production of the fistulas are diverticulitis and carcinoma. Simple, or so called self-limiting, diverticulitis may produce bladder symptoms occasionally and hence be the subject for differential diagnosis. When the inflammatory process extends beyond the wall of the diverticulum, peridiverticulitis with abscess formation occurs. The

Fig. 6. Case 5. Showing the presence of stones in the bladder; a case of vesico-enteric fistula.

abscess may rupture into the bladder, either with or without the formation of an enterovesical fistula. In one of our cases, after the abscess had ruptured into the bladder, the patient developed abscesses in the abdominal wall which required surgical intervention.

As an example of an enterovesical fistula due to the diverticulitis and peridiverticulitis, I should like to present the following case in which the patient also had stones in the urinary bladder:

CASE 5. (a) Enterovesical fistula; (b) chronic diverticulitis; (c) peridiverticulitis; (d) vesical calculi; (e) cystitis. W. N. H., male, aged 59, was admitted to the Presbyterian Hospital on June 28, 1936.

For the past 6 years the patient has had more or less indefinite pain in the abdomen. The pain was not constant. At this time he began to have some trouble with his bowels so that he had been more or less constipated. Sixteen months ago he noticed pain and burning on urination. There was some frequency of urination as well. Shortly after the onset of bladder symptoms the patient noticed the presence of small flakes in his urine. He then went to a doctor who told him he had fecal material in the urine. The patient also noticed passage of gas with the urine.

Examination of the eyes, ears, nose, throat, chest, and heart was negative. The rectal examination showed a 1 plus enlargement of the prostate and slight tenderness of the right lobe. Seminal vesicles were not palpable. Examination of the blood showed 4,250,000 red blood cells, 8,600 white blood cells, and a hemoglobin of 81 per cent. Examination of the urine on admission to the hospital showed no sugar, albumen, or blood. Sediment showed 240 leucocytes per cubic millimeter. Cultures revealed hemolytic Bacillus coli communior and small colonies of diplococci.

Cystoscopic examination showed the presence of an opening on the left lateral wall surrounded by some edema. There was slight intravesical enlargement of the prostate and on the floor of the bladder 2 large stones were seen.

Roentgenographic examination showed the presence of arthritis in the lumbar spine and 2 stones in the bladder (Fig. 6). Intravenous pyelograms were negative. Chest fluoroscopy was negative and the barium injection into the colon met an obstruction low in the sigmoid. No sinus was made out.

A litholapaxy was done on March 22, 1937, and a cystoscopic examination at the end of the operation showed the bladder to be free of stones and fragments of stone. Dr. Edwin Miller was asked to see the patient in consultation and he concurred in the diagnosis of diverticulitis with perforation into the bladder. A colostomy was performed by Dr. Miller on July 3, 1936.

Chemical examination of the stones revealed a mixture of calcium oxalate, carbonate, and triple phosphate with a trace of urates. The patient was discharged from the hospital on July 20, 1936.

Cancer of the rectum may occasionally perforate into the bladder with a resulting recto-vesical fistula. On the other hand, carcinoma of the prostate or bladder may involve the rectum with perforation with a resulting fistula between the bladder and the rectum. These situations, however, are rather uncommon and offer no difficulty in the way of diagnosis.

ACUTE PYELITIS FOLLOWING OPERATION

During the postoperative course following a major surgical operation, symptoms and signs may develop that are difficult to interpret and evaluate: (1) The clinical picture may be due to a lesion not recognized before operation and yet part of the primary pathology for which the patient was operated upon. (2) The clinical picture may be due to a lesion of the urinary tract, which, because of the absence of symptoms and signs was not recognized before operation, for instance the presence of a stone in the kidney or ureter, but following operation an acute pyelitis develops and the true condition in the urinary tract is then recognized. (3) A combination of symptoms that may be due in part to both conditions.

Under certain circumstances, it may be very difficult to decide which of the two lesions is the dominant one. This question may assume quite an important rôle in case one or the other lesion demands surgical intervention. Naturally, great care must be exercised in arriving at the proper conclusion as to whether the patient should be operated upon, and if so, which of the two lesions should be cared for first. An interesting problem bearing on this subject is presented in the following case:

CASE 6. (a) Carcinoma of the rectum; (b) metastasis to the liver; (c) stone in left kidney; (d) left hydronephrosis;

e) pyelitis. Mrs. S., aged 65, was admitted to the Presbyterian Hospital on the service of Dr. V. C. David, on May 24, 1938. The previous history was negative. The patient had always enjoyed good health until without apparent reason she suddenly began to feel weak. The weakness gradually increased. Several weeks later she began to have pain in the rectum and this was followed by a change in bowel habit. The patient suddenly developed a marked persistent diarrhea.

The physical examination was negative except for the presence of carcinoma of the rectum.

Examination of the blood showed 4,200,000 red blood cells, 10,500 white blood cells, and a hemoglobin of 80 per cent. The urinalysis on admission was negative.

A left inguinal colostomy was done by Dr. V. C. David on May 28, 1938, and a perineal resection on June 11, 1938.

Roentgenographic examination. The right pyelogram was normal. The left pyelogram showed dilatation and clubbing of the calyces and the presence of stones in the pelvis of the left kidney, presence of calcified glands near the spine, and calcifications in the spleen (Fig. 7).

Following the perineal resection the patient developed some fever. On the thirteenth day after operation examination of the urine showed the presence of a good deal of pus. On the twenty-fifth day the patient developed tenderness over the left kidney. The temperature continued to fluctuate between 100 to 103 degrees. Examination of the urine revealed a great deal of pus and there were 100 cubic centimeters of residual urine. Examination of the abdomen showed tenderness of the left kidney posteriorly, and the presence of a large palpable mass in the right upper quadrant. The mass was tender and the nature of it was indefinite. The diagnosis rested between enlargement of the liver and right-sided hydronephrosis.

The patient was treated with Mandelic acid and indwelling catheter drainage was instituted, but this had no effect on the temperature until an indwelling ureteral catheter was placed in the left ureter. This brought the temperature down immediately but 3 days later there was a sudden rise. Catheters were inserted in both ureters and left in place. This brought the temperature down and 5 days later the catheters were removed. The patient was discharged on July 27, 1938.

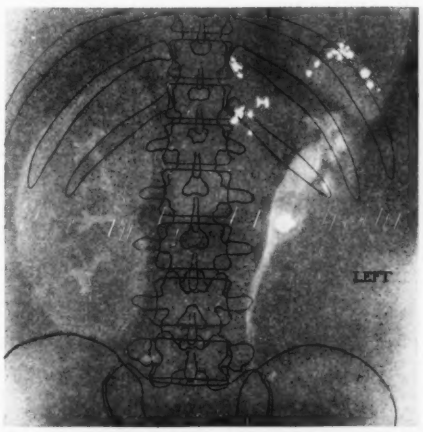

Fig. 7. Case 6. The right pyelogram was normal. The left pyelogram showed dilatation and clubbing of the calyces and the presence of stone in the pelvis of the left kidney, calcified glands near the spine, and calcifications in the spleen. Note enlarged right kidney.

LESIONS OF THE GYNECOLOGICAL TRACT

Various pathological conditions in the gynecological tract are often the cause of urinary symptoms. On the other hand, in some cases the patient may have disease in the urinary tract that is the direct cause of urinary symptoms, and with it may be associated conditions in the gynecological tract, such as prolapse of the uterus, cystocele, rectocele, fibroid, and various lesions of the tubes and ovaries. It is not at all an infrequent occurrence to see a patient in whom the urinary symptoms are erroneously attributed to the pelvic disease and for which the patient is operated upon without relief of the urinary symptoms. Among some of the more frequently overlooked lesions may be mentioned chronic pyelonephritis, hydronephrosis, renal and ureteral stone, renal tuberculosis, and elusive ulcer of the bladder. Just as the gynecologist should bear in mind the fact that his patient may also have a lesion in the urinary tract, so must the urologist bear in mind that his patient's symptoms may be due to a lesion in the gynecological tract. The necessity for a complete urological survey in this group is perfectly obvious. As an illustration of a patient belonging to this group, I wish to present the following case:

CASE 7. (a) Carcinoma of the right ovary; (b) fibromyoma of the uterus. Mrs. I. T., aged 50, was admitted to the Presbyterian Hospital on October 6, 1931. The previous history was negative. The patient consulted me because of pain in the back and frequency that she attributed to disease in the urinary tract. The present illness began 8 months before her admission to the hospital at which time she noticed pain in the right lumbar region. The pain gradually increased in severity and radiated toward the front. At times she also had pain in the right side of the abdomen low down. The pain was associated with an intense desire to void and kept her awake at night. It was relieved by urination. The patient was obliged to void 2 to 3 times at night and there was some increased frequency of urination during the day. Two months before admission she noticed a fullness in the epigastrium after eating. The bowels were constipated. There was no vaginal bleeding or discharge and no hematuria. Menopause had begun 6 months before.

Physical examination was made by Dr. E. E. Irons. Examination of the head, neck, heart, and lungs was negative. There was some tenderness on deep pressure over the right kidney. Vaginal examination showed a mass the size of a small orange to the right of the uterus, which was about twice its normal size. Examination of the urine was negative except for the presence of a few white blood cells. The blood count showed 4,010,000 red blood cells, 26,600 white blood cells, and a hemoglobin of 62 per cent. The blood pressure was systolic 132 and diastolic 82.

Roentgenographic examination was negative for stone. Intravenous urograms were negative. Chest fluoroscopy, gastro-intestinal studies, and gall bladder were negative.

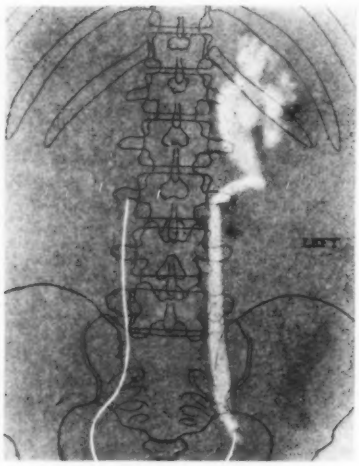

Fig. 8. Case 8. Hydronephrosis and hydro-ureter due to carcinoma of the ovary.

On October 12, 1931, Dr. N. S. Heaney performed a bilateral salpingo-oophorectomy and a supravaginal hysterectomy.

Pathological diagnosis. Krukenberg tumor of the right ovary and fibroids of the uterus.

In this case, although there were no especial problems in the diagnosis, the symptoms which brought the patient to me were essentially urological and there were no symptoms referrable to the gynecological tract. The urological symptoms, namely, pain in the right lumbar region, that radiated forward, pain in the right lower quadrant, and frequency of urination gave the clinical picture a decidedly urological aspect; however, with the negative findings from the urological point of view plus the results of the pelvic examination the diagnosis was relatively simple.

Pain in the left upper quadrant occurs much less frequently than it does on the right side, and as a rule it offers fewer problems in differential diagnosis than do lesions on the right side. In other words, with fewer organs on the left side than on the right, there is less pathology and consequently fewer diagnostic problems. However, lesions do occur that present a clinical picture that is not always perfectly clear, and it is necessary to differentiate lesions of the colon, kidney, and spleen. I should like to present the following case as an illustration:

Case 8. (a) Left hydronephrosis; (b) left hydro-ureter; (c) papillary carcinoma of the ovary. Mrs. M. D., aged 36, was admitted to the Presbyterian Hospital on October 11, 1938, on the service of Dr. J. B. Eyerly. Her complaints on admission were abdominal distress, menorrhagia, frequency of urination, and loss of weight. The patient stated that she was operated on for a dermoid cyst of the left ovary in June, 1937, at which time the left fallopian tube and appendix were removed, and that following this operation she experienced an indefinite, dragging and pulling sensation at the lower end of the operative scar. The patient complained of an abdominal distress which she described as a "bloated" feeling in the abdomen. Constipation began 2 months after her operation with hard bowel movements. She also complained of a dull aching sensation in the left side of the abdomen. This pain had been present more or less constantly and increased gradually in severity, disappearing before the onset of menstruation and reappearing following menstruation. In the beginning of October, 1938, the patient began to have frequency of urination, both day and night.

Physical examination was made by Dr. J. B. Eyerly. Examination of the heart, lungs, head, and neck was negative. A vaginal examination by Dr. N. S. Heaney showed a swelling the size of a hen's egg on the left side, in the region of the uterine artery, extending from the side wall of the uterus to the pelvis and involving the sacro-iliac ligament. The blood pressure was systolic 154 and diastolic 100.

The urinalysis on admission showed the urine to be normal. The blood count showed 4,200,000 red blood cells and 11,650 white blood cells. The blood chemistry showed urea nitrogen, 11; uric acid, 3.8; creatinin, 1.4; and non-protein-nitrogen, 27. Phenolsulfonphthalein test showed an output of 80 per cent in 3 hours.

The cystoscopic examination on October 14, 1938, showed a normal bladder. The right ureter was catheterized without difficulty or obstruction. There was some obstruction to the passage of the catheter up the left ureter. The urines from the right and left kidneys as well as the bladder were free of pus and sterile on culture.

Roentgenographic films were negative for stone. The right pyelogram was normal. The left pyelogram showed dilatation of the kidney pelvis, calyces, and ureter. The dilatation of the ureter stopped at a point below the left sacro-iliac joint (Fig. 8).

Because of the presence of an obstruction in the left ureter with secondary hydronephrosis and pain in the left side of the abdomen, preliminary dilatation of the ureter was carried out prior to the operation. After several dilatations the patient developed an acute pyelitis, for which indwelling ureteral catheter drainage was carried out. A colpotomy was performed by Dr. N. S. Heaney on October 24, 1938. Examination of the pieces removed showed papillary carcinoma. Subsequently, the patient was given radium implantation of 2,100 milligram hours, and was discharged on December 1, 1938.

LESIONS OF THE SPINE

Because of the fact that pain in the back is not always of renal origin, it is necessary that the urologist, in his consideration of differential diagnosis, bear in mind the fact that the patient may have a lesion of the spinal column. It is not necessary in this symposium to consider all the lesions of the spine that may be confused with lesions of the kidney, but I wish to call attention to 3 of them: (1) arthritis; (2) lesions of the vertebræ, and (3) prolapse of nuclear pulp.

1. *Arthritis.* Although a relatively common cause of pain in the back that brings the patient

to the urologist, arthritis as a rule presents no serious problem in differential diagnosis

2. *Lesions of the vertebræ.* Osteomyelitis of the spine is a relatively uncommon lesion, and it has been overlooked in several cases under recent observation. In some instances the only manifestation of osteomyelitis is pain in the back. In other instances it may manifest itself in the form of a perirenal abscess. Therefore, it is well always to bear in mind the possibility that a perirenal abscess may be due to an osteomyelitis of the spine.

As a rule the diagnosis of a perirenal abscess is relatively easy, especially in the later stages, and is based on the presence of pain in the back, fever, leucocytosis, muscular rigidity, and a palpable swelling. On the other hand, pain in the back leucocytosis, fever, and muscular rigidity may also be due to osteomyelitis of the vertebræ.

Because of the fact that osteomyelitis of the spine may be the cause of perinephritic abscess, it is well to bear this possibility in mind and to consider it as a factor in every case of perirenal abscess. As an example of a case in which osteomyelitis of the spine was overlooked for a long time in a patient who was operated upon for a perinephritic abscess before he came to me, I should like to present the following:

CASE 9. (a) Subacute osteomyelitis of the lumbar spine; (b) osteoarthritis of the spine; (c) right lumbar incisional hernia; (d) secondary anemia; (e) bilateral pyelonephritis. H. L., male, aged 57, was admitted to the Presbyterian Hospital on December 12, 1934. The patient was in good health until 4 months before his admission to the hospital at which time he complained of pain in the right upper quadrant that radiated to the back. He was admitted to a hospital where a diagnosis of bilateral bronchopneumonia was made. A few days later he developed pus in the urine and he began to run a septic type of temperature. The pyuria increased and he developed tenderness in the right renal area. A diagnosis of right perinephritic abscess was made and he was operated upon. He was discharged from this hospital 3 weeks after operation.

Shortly thereafter he developed pain in the left side localized on a level with the third lumbar vertebra and he again began to run a septic temperature. He was readmitted to a second hospital where he remained for a short time and then was sent to a convalescent home. The pain in his left lumbar area continued, however, as did the fever and pus in the urine and he was sent to the Presbyterian Hospital.

The physical examination revealed a poorly nourished male who was in severe pain. Examination of the heart and the lungs was essentially negative. The abdomen showed a recently healed scar in the right renal area and a hernia in the lower end. There was a localized point of tenderness to the left of the spinal column and at the level of the last rib. The rectal examination was negative.

The urine on admission showed some albumen and 2,401 leucocytes per cubic millimeter. The blood count showed 3,870,000 red blood cells and 12,400 white blood cells. The blood chemistry tests were negative.

Fig. 9. Case 9. Note changes at the third lumbar due to osteomyelitis of the spine.

The cystoscopic examination was negative. The ureters were catheterized without difficulty or obstruction. The urine from the right kidney was free of pus and sterile upon culture. The urine from the left kidney showed 5,600 leucocytes per cubic millimeter and cultures showed hemolytic and non-hemolytic Staphylococcus aureus. Bladder urine showed 640 leucocytes per cubic millimeter and hemolytic and non-hemolytic Staphylococcus aureus. Smears of the urine were negative for tubercle bacilli.

Roentgenographic examination. The films were negative for stone. The right pyelogram was negative and the left showed a slight dilatation of the pelvis and slight clubbing of the calyces. The roentgenogram showed a destructive lesion involving the body of the third lumbar vertebra (Fig. 9).

A diagnosis of osteomyelitis of the body of the third lumbar vertebra was made. Dr. Kellogg Speed was asked to see this patient in consultation and he concurred in the diagnosis. From the evidence obtained a diagnosis of subacute osteomyelitis of the body of the third lumbar vertebra was made and appropriate orthopedic treatment instituted; the patient made a complete recovery and was discharged on December 26, 1934.

3. *Prolapse of nuclear pulp.* During the past few years many articles dealing with prolapse of the nuclear pulp, or Schmorl's disease, have appeared in the literature so that it is not necessary to enter into a detailed discussion or description of this relatively recently described condition. Of prime importance, as far as the urologist is concerned, is the fact that he should constantly bear in mind the possibility that it may be the cause of pain in the back and he should not fail to have a lateral roentgenogram made of the spine. This is now a routine procedure even when obvious pathology in the urinary tract is present, since it is possible in some of these cases that both lesions may be present at the same time. I should like to present the following case as an example:

Fig. 10. Case 10. Calcified nuclear pulp at intravertebral discs.

CASE 10. (a) Congenital solitary kidney, right; (b) hydronephrosis, right; (c) hydro-ureter, right; (d) bifid kidney pelvis, right; (e) prolapse of nuclear pulp. Mrs. S., aged 44, was admitted to the Presbyterian Hospital on January 22, 1936. The past history was negative. Her complaints began about 6 weeks before consultation, at which time she had frequency of urination and some burning in the urethra. The patient also noticed that her urine was dark and cloudy and on examination it showed a small amount of blood and considerable pus. The blood cleared up in 2 or 3 days and has not again appeared. The patient also complained of pain in the back. She had been treated with pelvic lavage elsewhere.

Examination of the heart, lungs, head, and neck was negative. The liver and right kidney were palpable and there was no lumbar tenderness. A pelvic examination revealed an infantile uterus. The blood pressure was systolic 124 and diastolic 82.

The blood count and blood chemistry were negative. Examination of the urine on admission was negative. Phenolsulfonphthalein showed an output of 80 per cent in 1½ hours.

The cystoscopic examination showed a normal bladder. The right ureteral orifice was normal in size, shape, and position. No left ureteral orifice was found after very careful search. Examination of the bladder urine showed no pus. Cultures showed Bacillus coli. Guinea pig inoculations were negative for tuberculosis.

Roentgenographic examination. The plain film was negative for stone. The right kidney outline was very large, extending from the fifth lumbar to the twelfth dorsal. The kidney outline on the left side was not visualized. Intravenous pyelograms showed a very large right kidney pelvis with a possible slight dilatation of the right ureter. There was no visualization on the left side. A lateral film showed a rather unusual type of calcification at the intervertebral discs. Instead of one large island of calcification centering two-thirds of the way back in the disc one sees many smaller islands at the junction of the second, third, fourth, and fifth which center two-thirds of the way forward in the disc. In addition the margins of vertebræ are cup-shaped as in nuclear pulp enlargement (Fig. 10). The patient was discharged from the hospital on January 25, 1936.

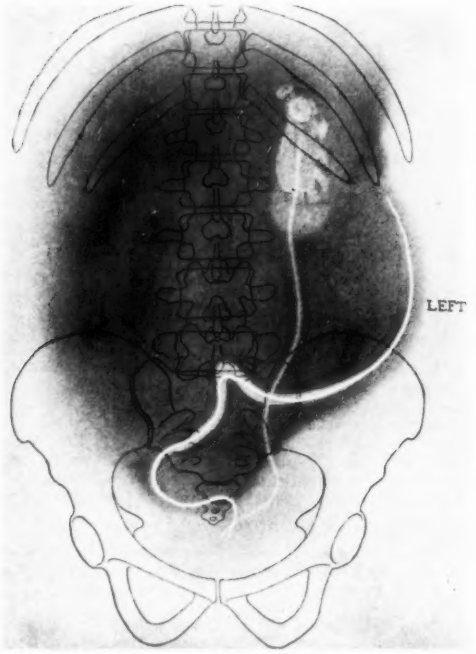

Fig. 11. Case 11. Note displacement of the catheter in the right ureter and small hydronephrosis of the left kidney. The shadow produced by the hydronephrosis nearly fills the abdomen.

Following the acute onset of urinary symptoms a diagnosis of acute pyelitis was made, appropriate treatment was carried out, and the condition cured. However, the pain in the back continued and it was for the persistence of pain that the patient consulted me.

Pain in the back is often associated with acute renal infection, and it disappears when the infection is cured. Therefore, its persistence should always arouse our suspicions that the patient must have some other type of pathology that explains the cause of the symptoms, which in this case was demonstrated with a lateral roentgenogram.

HYDRONEPHROSIS

Hydronephrosis is one of the common lesions of the kidney that is frequently overlooked and confused with various intra-abdominal lesions. In some cases there are no symptoms referable to the kidney and the hydronephrosis is discovered only upon routine examination. In other instances the only manifestation of hydronephrosis is indefinite pain in the abdomen, the cause of

which is not recognized, and, in some cases an abdominal operation is performed without relief of symptoms.

Because of the large size of the hydronephrosis, the condition may be confused with various types of intra-abdominal swellings. In another group of cases the patient may develop severe pain, which may even result in shock and collapse, so that the clinical picture is that of an acute intra-abdominal emergency. As an example, I should like to present the following case:

CASE 11. Bilateral hydronephrosis. W. S., male, aged 24, was admitted to the Presbyterian Hospital on July 29, 1937, on the service of Dr. William Kirby.

The patient complained of a mass in the abdomen which he said had been present for 2 years. Three years before his admission to the hospital the patient had a severe fall at which time he had severe abdominal pain. The next day he noticed that his urine was very bloody. The hematuria continued for 10 days. Two years before his admission to the hospital he was in an automobile accident, was unconscious and again passed bloody urine for 10 days. Since the second accident the patient noticed the presence of a mass in the abdomen which gradually increased in size. The swelling had become more noticeable during the past 6 months.

Examination of the heart, lungs, head, and neck was normal. The abdomen appeared distended and the right half was much more prominent than the left. The right costal arch was elevated and the maximum fullness appeared to come out from under the arched ribs. A superficial vein was visible on the right side of the abdomen running from the costal arch down to the level of the umbilicus. The entire abdomen was very tense except for a small area in the lower left quadrant. There was no pain or tenderness and one gained the impression that the mass was cystic and not solid. The blood pressure was systolic 174 and diastolic 110.

Examination of the urine showed no sugar or albumen; an occasional red blood cell was seen and there were 140 white blood cells per cubic millimeter. There were a few granular casts in the urine. The blood count revealed 6,270,000 red blood cells, 12,000 white blood cells, and a hemoglobin of 98 per cent. A Wassermann test was negative. Blood chemistry showed: urea nitrogen, 14.0; uric acid, 4.3; non-protein-nitrogen, 36.5.

The cystoscopic examination was normal. The ureters were catheterized without difficulty or obstruction. The urines from the right and left kidneys as well as the bladder were free of pus cells. The urine from the right kidney contained a few red cells and cultures were sterile all around.

A roentgenographic examination on August 3, 1937, showed no evidence of stone in the urinary tract. The kidney outlines were obscured by a large soft parts' shadow that nearly filled the entire abdomen. The right ureter catheter passed upward toward the top of the sacrum and from this point it curved to the left so that it lay at the left border of the previously described shadow. The left ureteral catheter followed a normal course (Fig. 11). The left pyelogram showed the presence of a small hydronephrosis. No outline of the right pelvis could be demonstrated in the x-ray film.

Seven days after admission to the Presbyterian Hospital, the patient developed a sudden severe attack of pain. There was a rapid increase in the size of the abdomen. The pulse rose from 76 to 126 and the temperature to 102 degrees. The patient had severe nausea and vomiting and the pain increased in severity and was only slightly relieved by a hypodermic injection of morphine. He rapidly went into shock and collapse and it was necessary to give him a blood transfusion. In addition he was given intravenous injections of glucose and external applications of heat. The patient gradually improved and a right nephrectomy was done on August 6, 1937. Because of the enormous size of the hydronephrosis it was necessary to aspirate it. The fluid removed measured 6,100 cubic centimeters and was dark in color due to the presence of old blood. The patient made an uneventful recovery and was discharged on September 1, 1937.

This patient presented a rather interesting problem in differential diagnosis because of the sudden onset of the severe pain which was followed by shock and collapse and because of the increased rigidity of the abdominal wall. This sudden change in the clinical picture immediately raised the question of the possibility of our dealing with a double lesion, and that the patient besides his hydronephrosis might have any one of the following lesions: acute pancreatitis, mesenteric thrombosis, acute intestinal obstruction, or perforation of a hallow viscus, such as rupture of a gastric or duodenal ulcer or an acute gangrenous gall bladder.

RETROPERITONEAL TUMORS

It is a well known fact that retroperitoneal tumors produce no typical clinical symptoms by means of which they can be recognized, and, that as a rule, when the patient is seen, the tumor has reached a large size. In an occasional case the tumor is discovered after the patient has received an injury, and in other instances the only complaint is that of indefinite pain.

Retroperitoneal tumors are often confused with lesions of the kidney, adrenal, pancreas, and Riedel's lobe of the liver. A complete urological study is always indicated and is most informative. Ureteral catheterization and retrograde pyelograms show two common findings that are of great value, namely, displacement of the kidney pelvis, with or without changes in the pyelogram, and changes in the course of the ureter. As an illustration of a patient in whom both of these findings were present, I should like to present the following case:

CASE 12. (a) Retroperitoneal fibrosarcoma. Mrs. A. S., aged 64, was admitted to the Presbyterian Hospital on the service of Dr. William A. Thomas. The previous history was negative. The patient on admission to the hospital complained of right-sided, low backache which was gradual in onset. It was described as a dull ache, never severe nor colicky in nature, which was relieved by lying down and by heat and aspirin. There were no urinary symptoms.

The heart, lungs, head, and neck were negative. Examination of the abdomen revealed a hard smooth mass in the right mid-abdomen, about the size of an orange and

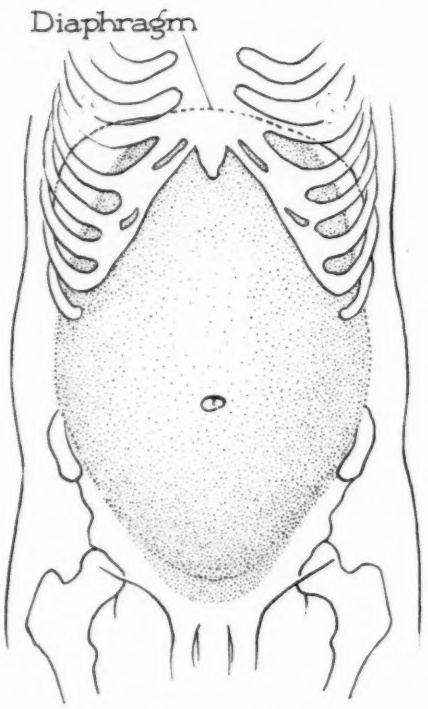

Fig. 12. Enormous dilatation of the urinary bladder due to obstruction at the bladder neck.

there was some respiratory mobility. There was no tenderness. The vaginal examination was negative. Examination of the blood, urine, and stomach content was proved to be normal.

Cystoscopic examination showed a normal bladder. The ureters were catheterized without difficulty or obstruction. The urines from the right and left kidneys as well as the bladder were free of pus and sterile on culture. Smears revealed no tubercle bacilli.

Roentgenographic examination. The examination was negative for stone in the urinary tract. The right pyelogram showed a normal pelvis except that the pyelogram was tilted outward and to the right. The right ureter curved outward and to the right and there was slight dilatation of the right ureter over the sacrum. The left pyelogram was normal. A large, irregularly rounded or nodular soft tissue density was seen filling the right side of the abdomen. This shadow extended from the lower edge of the eleventh rib to the mid part of the sacro-iliac joint and from the right margin of the spine laterally to the edge of the film.

An operation was performed on October 24, 1935, by Dr. E. M. Miller and Dr. H. L. Kretschmer. Laparotomy showed a retroperitoneal tumor mass and the sections removed showed the presence of a fibrosarcoma. The patient made an uneventful recovery and was discharged from the hospital on November 24, 1935.

From the careful pre-operative study, it was perfectly obvious that we were dealing with a retroperitoneal tumor probably malignant, and that the tumor mass was extra-urinary. The presence of a normal pyelogram which was tilted, the tilting of the kidney, the dislocation of the right ureter with a normal pyelogram, left little room for doubt that the tumor was retroperitoneal and not connected with the kidney.

ELUSIVE ULCER

One of the lesions of the urinary tract frequently confused with lesions of the lower abdomen is the so called elusive ulcer. This condition is relatively uncommon, yet it occurs with enough frequency to justify bearing it in mind in the differential diagnosis of lesions of the lower abdomen. Unfortunately, this lesion is not taken into consideration frequently enough, with the net result that many of these patients are not seen until after they have had a prolonged course of local treatment, or until after they have had one or more abdominal operations without avail. In many of these cases the symptoms are attributed to a diseased appendix and an appendectomy is done. In another group various gynecological procedures are carried out without relieving the symptoms in any way.

It is in this group of cases that the value of a history is apparent. When a patient states that she has frequency of urination, urgency, and severe bladder pain, and if the symptoms have not been relieved by various forms of local treatment or by one or more surgical operations, we make a working diagnosis of elusive ulcer. These cases are overlooked because we fail to bear this possibility in mind, during the differential diagnosis. It is to be remembered that in probably the majority of them the urine is clear and sparkling and the urinary examination may be negative. The diagnosis rests upon the cystoscopic examination, the findings being quite characteristic.

DIFFERENTIATION BETWEEN ASCITES AND CHRONIC URINARY RETENTION

As a rule lesions of the bladder, such as stones, tumors, ulcer, and vesical neck obstruction are not very frequently confused with intra-abdominal lesions and it is relatively rare that they are considered in the problems of differential diagnosis between abdominal and urinary disease. A chronically distended bladder may reach such an enormous size that the full bladder may be confused with ascites. At times difficulty may arise in making a differentiation between ascites and an overdistended bladder.

The presence of a suprapubic tumor due to chronic urinary retention as a rule does not present any special problems in differential diagnosis. A long standing history of urinary obstruction, the rather characteristic outline or shape of the swelling, and the results of catheterization suffice to establish the diagnosis.

When the distention of the urinary bladder reaches to or above the xiphoid cartilage (Fig. 12), this condition may be and has been confused with ascites. In cases of this kind there is extensive displacement of the intestines just as occurs in ascites which adds to the diagnostic problem.

Urinary symptoms when present may be ascribed to the ascites, it being assumed that the ascites mechanically interferes with the act of micturition. The differentiation between ascites and chronic urinary retention of this magnitude rests upon the results of catheterization. It is needless to emphasize that the removal of the urine must be done very slowly and under close observation.

SUMMARY

The rôle of the urologist is a very important one in the differential diagnosis of abdominal disease. He must be familiar with the various types of intraperitoneal, as well as retroperitoneal lesions that may be confused with lesions of the genito-urinary tract. It is most important that he be familiar with complications that arise following general and gynecological surgical procedures.

A CLINICAL STUDY OF ALLOY STEEL WIRE SUTURES IN HERNIA REPAIR

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THERE is general agreement among surgeons that for satisfactory wound healing the rôle of the materials employed for ligatures and sutures is of particular importance. Such materials should be sterile and pliable, fine and delicate in texture, with such tensile strength as to maintain approximation of tissues without prolonged or excessive irritation. The relative value of absorbable and non-absorbable sutures has long been a subject of discussion, and the discussion has largely been concerned with silk and catgut. Catgut continues to be generally favored by surgeons by reason of the emphasis placed upon absorbability as the decisive element in satisfactory wound closure, and, therefore, it still remains our standard material. However, its absorbability frequently gives rise to serious complications in wound healing, since in some cases it may fail to persist long enough to accomplish its purpose of coaptation until union may occur. In other cases its absorption is so long delayed that its reaction is that of a non-absorbable suture.

Kraissl, in a thorough review of the subject, has stressed the many inadequacies of the absorbable suture materials, particularly with reference to the problem of wound disruption. Kraissl, Babcock, and others have demonstrated catgut allergy and its deleterious effects on wound healing. Clock has shown the dangers of unsterile catgut in studies of standard brands of catgut; furthermore, he has demonstrated the disadvantages of processing by chemical sterilization.

Recently interest has been stimulated in the use of non-absorbable suture materials, and particularly wire. Silver wire was successfully used by Shipley in the secondary repair of operative wound disruptions. Reid, Zinninger, and Merril reported an extensive use of silver wire in the closure of the abdomen in cases of acute abdominal emergencies, particularly in the presence of great tension, marked tissue friability, probability of infection, or marked general debility. Their technique consisted in the use of interrupted through-and-through sutures of all abdominal layers, these sutures being removed in 15 to 20 days. In a large series of cases studied over a 10-year period, there were no wound disruptions and a markedly decreased incidence of post-operative hernia.

Stainless alloy steel wire, as described by Babcock, has numerous advantages over silver wire, and is gaining popularity as experience in its use enlarges the zone of its application. It does not tarnish or corrode, and consequently does not produce tissue discoloration; has greater tensile strength and is less brittle than silver wire; is absolutely impermeable and easily manipulated. Its use in fine sizes permits accurate layer-for-layer closure in the form of buried sutures, and easy applicability in the ligature of vessels. It is easily sterilized and relatively inexpensive.

Dambrin has used alloy steel wire sutures in abdominal closures over a long period of years, using a two-layer technique: a deep, buried layer of figure-of-eight sutures for fascia, muscle, muscle sheath and peritoneum and a superficial layer of removable steel wires. He was impressed with several observations: (1) the absence of post-operative discomfort at the site of buried sutures; (2) the fact that, even when wounds became grossly infected exposing the deep layer of wire sutures, the sutures remained intact with firm healing after control of the infection; (3) the complete absence of wound disruption; (4) the fact that these patients could be exposed to diathermy or x-ray without any untoward results. De Mendonca reports the use of alloy steel wire in an extensive series of cases. He has used wire exclusively in vesicovaginal fistulas, uranoplasties, perineorrhaphies, hernias, and abdominal wall repairs. He, too, was impressed with the fact that even in the presence of severe infection and prolonged drainage, wire sutures remained intact and maintained firm coaptation of tissues. H. Welti emphasized the following advantages of alloy steel wire buried sutures: (1) they are inoxidizable and therefore cause minimal tissue reaction; (2) the unusual tensile strength of alloy steel wire permits its use in very fine sizes, therefore reducing the bulk of buried suture material.

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In an attempt to clarify the status of alloy steel wire sutures, we conducted two investigations which form the basis of this paper: (1) a study of 56 consecutive cases of hernia repairs; (2) a study of wound repair in dogs.

A. THE STUDY OF HERNIA REPAIRS

In this series of 56 consecutive hernia operations at the Metropolitan Hospital and the Flower and Fifth Avenue Hospital, suture materials were used in the following groupings: Group 1—25 cases—catgut, chromicized and plain, was used throughout for buried sutures. Group 2—18 cases—alloy steel wire sutures used for repair of the anatomical structural defects, with catgut for the peritoneal sac and hemostatic ligatures. Group 3—10 cases—alloy steel wire sutures were used exclusively throughout, including repair of the defect, peritoneal sac, and hemostatic ligatures. Group 4—3 cases—black silk was used throughout, including peritoneum and ligatures.

The plain catgut, chromicized catgut, and black silk were of the usual standards and sizes and were employed in standard technique. The stainless alloy steel wire was used in two sizes: the No. 35 B&S gauge (0.0007 inch), with a tensile strength of 2½ pounds, was employed for ligature ties and delicate approximating; the No. 30 B&S gauge, with a tensile strength of 15 pounds, was used for supporting structures (closing hernia defects). The wire was handled as were other suture materials; care was taken not to kink the wire, and ends were cut close to the knot and flattened wherever possible. The wire was usually employed as an interrupted suture but in several instances we have employed the fine wire as a continuous suture. For supporting structures (such as approximating conjoined tendon to Poupart's ligament), double strands of No. 35 wire were used in many of the cases.

All clinical case groups were closely observed during the immediate postoperative course. The operative wounds were classified as follows: (1) *clean*, absence of infection; (2) *infected*, gross evidence of pus, requiring drainage; (3) presence of *seroma*, that is, our clinical designation of a gross accumulation of serum or blood requiring evacuation, without subsequent suppuration. At the time of discharge from the hospital, each wound was carefully examined with the purpose of determining the relative amounts of wound induration in the various suture-type cases. Again, approximately 1 year after this study was initiated, all cases were brought back for a follow-up examination. The time elapsed between date of operation and date of follow-up examination varied from 2 to 10 months. At this time each patient was examined with an attempt to determine: (a), the relative amount of wound induration; (b) recurrence or weakness; (c) any symptomatic complaints referable to the type of suture material used.

ANALYSIS OF CLINICAL CASE GROUPS

Types of hernia. In this series of 56 cases, 42 were elective inguinal operations, 1 a strangulated inguinal (emergency) operation, 1 a strangulated femoral (emergency) operation, 8 postoperative incisional hernia (ventral) repairs, and 4 recurrent inguinal repairs.

Incidence of infection. In group 1, catgut sutures, in 25 operations, there were 6 infections, an incidence of infection of 24 per cent. In group 2, combined catgut and wire, there were 18 operations, with 2 infections, an incidence of infection of 11 per cent. In group 3, *wire exclusively*, there were no infections in the 10 operations. In group 4, black silk exclusively, of 3 operations there were 2 infections.

We wish to stress at this point that the incidence of suppuration in these 3 cases in group 4 is rather the exception to our satisfactory experience with the use of black silk in many other types of clean cases. In our experience the use of fine silk in wounds closed without drainage has been attended by a low incidence of suppuration; but the 2 cases in which infections occurred were secondary repairs of very extensive ventral incisional hernias and because of a large amount of dissection and considerable oozing, were closed with drainage, with catgut employed for ligatures. Halstead many years ago stressed the necessity for accurate hemostasis and the absence of drainage for exhibition of silk in wound repair.

Incidence of seroma. In group 1, no seromas occurred. In group 2, 5 seromas occurred in 18 operations, an incidence of 27 per cent. In group 3 there were no seromas. In group 4, 1 seroma occurred in 3 operations, an incidence of 33 per cent.

Degree of wound induration. We realize that wound induration is a matter of individual interpretation, but since all cases were observed by the three authors, we feel that the interpretations were relatively fair. At the time of discharge from the hospital following operation the wound induration in groups 2 and 3 (that is, all cases in which wire sutures were used either entirely or in major part) was definitely less than in the catgut or black silk groups. At the time of follow-up examination, however (2 to 10 months later), the various suture type cases could not be distin-

guished from one another from the standpoint of relative wound induration.

Recurrences. At the time of follow-up examination there was only 1 recurrence and that was in a black silk repair of an incisional hernia with severe wound infection. Because of the short period of time elapsed, however, we feel that no value can be attached to the report of recurrences.

Symptomatic patient complaints. There were no complaints of discomfort, sticking, or pricking sensations referable to the use of steel wire sutures.

B. THE STUDY OF WOUND REPAIR IN DOGS

Recently we attempted by means of animal investigation to ascertain whether or not our clinical impressions of alloy steel wire sutures could be confirmed under the microscope. It was therefore necessary to determine the tissue reaction of an individual animal to various types of suture material. The experiment was carried out on dogs as follows: The abdomen of each dog was divided into four quadrants. In each of these quadrants, under aseptic technique, an operative incision was made in the anterior abdominal wall extending through the peritoneum. The wounds of the two right quadrants were closed layer-by-layer, throughout, with interrupted sutures of No. 35 gauge alloy steel wire, wire also being used for all ligature ties. The incision in the left upper quadrant was closed in the same manner with black silk throughout. The incision in the left lower quadrant was closed with No. 1 chromic catgut. The tissues of the one dog were thus subjected to the foreign body effects of the various suture materials. At varying time intervals of 4, 8, 12, 16, and 20 days the dogs were re-operated upon and the suture-line areas excised *en bloc*, including skin through peritoneum. The gaping defects left in the abdominal walls by these procedures were then closed with through-and-through interrupted sutures of alloy steel wire, which were subsequently removed.

During the course of the experiment we were again impressed with the observation that the wounds closed with wire healed more rapidly and with less induration, redness, and swelling than the wounds which were closed with either black silk or catgut. The clinical observation of the experimental wounds healing gave us the same results as we had observed in the healing of wounds among our patients. In only one instance did gross infection of an incision occur. This happened in a right lower quadrant wound following a secondary closure under marked tension, of a large tissue "block" defect after removal of an abdominal wall section. We were impressed with the rapid healing which occurred in this wound following control of the infection; 8 days after the infection was first discovered and treatment instituted, the wound was completely healed, the infection was cleared up and healing proceeded without the removal of any of the wire sutures. There were no cases of evisceration, no weak scars or hernia, and all the dogs survived operation and re-operation.

As the "blocks" of tissue were removed from the animals they were brought to the surgical pathological laboratory where sections including all the layers of the abdominal wall were made. The slides thus prepared were examined in an attempt to determine whether or not there were quantitative or qualitative differences in the tissue reactions of the individual dog to the presence of the various suture materials; and also, whether microscopy could reveal the extent of healing in the various instances. The findings as reported by Dr. L. C. Reid of the department of surgical pathology were as follows: "Those specimens containing the alloy steel wire showed less necrosis and less inflammatory exudate than the sections containing either the silk or catgut. The degree of proliferative reaction and fibrous tissue replacements in the wire sections parallel closely the findings in the silk sections; and these two are further advanced than similar reactions shown in the sections from the catgut wounds."

It is evident that exact differences of tissue reaction in the dog to various suture materials could not be demonstrated microscopically. Furthermore, the various day-interval specimens of tissue offered no additional microscopic information of significance in this immediate problem of suture material reaction in the dog.

SUMMARY

1. The use of buried steel wire sutures in a series of hernia repairs has resulted in a marked reduction of wound infections.

2. When wire is used in the same wound with absorbable suture materials, there is a marked tendency to seroma formation.

3. Whenever possible, therefore, it is advisable that wire suture material should be used exclusively and not with absorbable suture material in the same wound.

4. Despite the presence of infection in cases in which wire was used in combination with catgut sutures, all the wire sutures remained intact throughout the process of wound healing.

5. During the immediate postoperative course, there was distinctly less induration, redness, and

swelling in the wire cases than in those of other suture materials.

6. Two to 10 months later, however, the wire wounds were practically indistinguishable from those in which other suture materials were used.

7. Patients have manifested no untoward or uncomfortable symptoms referable to the presence of buried wire sutures in the tissues.

8. A study of tissue reactions in dogs to the various suture materials has in general borne out our clinical impressions of alloy steel wire.

9. The results of these investigations warrant the further use of alloy steel wire sutures.

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INGUINAL HERNIA

Application of Cardinal Principles in the Repair of Inguinal Hernias

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WE are endeavoring in this article to discuss and present in a clear-cut manner a method of repair of hernias in the inguinal regions which in our hands has been quite successful. This method differs in a few essential points from others described in textbooks and recent surgical literature (1, 5, 6, 7, 13, 19.). In it we are stressing a few important points in the proper repair of inguinal hernias which have been emphasized at one time or another by different competent workers in the surgical field (1, 5, 6, 7, 10, 13, 16). There is nothing original in this new type of repair of inguinal hernias described later in this article, as the principles involved have been thoroughly proved of value in the experimental as well as in the practical field by other observers and workers. However, it is our belief that this is the first instance in which a technique for repair of inguinal hernias is presented and described where these principles are well correlated and incorporated in a single simple method of reconstruction of hernial defects in these regions. Recently Zimmerman described a method of his own which is the nearest one in similarity to ours as far as we have been able to determine by reviewing the literature of the last three decades on the subject of "Repair of Inguinal Hernias." However, there are some points in Zimmerman's method which are disregarded, such as the excision of the direct sac or sacs and the final placement of the cord and which we consider of paramount importance in the proper correction of inguinal hernial defects. The few variations shown at the time of the description of the operative technique demonstrate the flexibility and applicability of this method to most of the problems encountered by the surgeon at the time of the operation for hernias in these regions.

Inguinal hernias are divided for anatomical purposes into three main varieties, indirect, direct and femoral, depending on the relative position of the component hernial peritoneal sac or locule to the deep epigastric vessels and femoral canal (Fig. 1). It is obvious that according to this type of classification a femoral hernia is simply a variation of the direct type of defect in which the peritoneal sac or locule insinuates itself in the femoral canal. Unilocular, indirect hernias occur frequently in children and very young adults. This fact is easily explained by the anatomical variations and arrangement of internal viscera characteristic of this age group. In our experience chiefly with male patients above the age of 35 years, we have rarely encountered this type of hernial defect. Most of the indirect hernial defects in our large series of patients operated upon have consistently presented a definite direct sac or locule which made the type of defects encountered a mixed one, indirect-direct type or bilocular type (Fig. 2). This finding has been corroborated with very few exceptions through the routine digital exploration of the peritoneal under surface of the floor of the canal and the subsequent dissection of the direct locule or sac from its attachment to the under surface of the floor of the canal and lateral wall of the urinary bladder. Unilocular direct hernias, excepting in recurrences, have been similarly rarely encountered as invariably a small demonstrable indirect sac or locule has been found easily and dissected from its attachment to the cord and under brim of the muscular internal ring. The direct type of hernia in which the sac or locule projects itself through the relaxed femoral ring is also included in the last group mentioned.

Based on our findings at the time of operation we have been classifying hernias in the inguinal regions according to the number of locules found and radically dissected: monolocular hernias which are rare; bilocular hernias which are very frequent; and the rarer trilocular hernias (indirect-direct femoral or indirect with two separate direct locules). According to this simple classification of inguinal hernias a bilocular hernial defect may be composed of an indirect sac with a true direct simple sac or with a concomitant direct sac projecting into the relaxed femoral canal. Accompanying any of these types of inguinal hernias there may be, too, associated pseudohernias, such as diverticula and fatty masses. The diverticula are frequently found in or near the inguinal triangle (3), and are usually mistaken and classified as direct hernial defects when in reality they are

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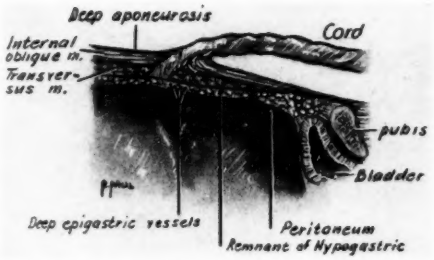

Fig. 1. Schematic oblique sagittal section in inguinal region as seen from inner aspect, illustrating peritoneal relations encountered in a normal specimen. Note the location of the epigastric vessels, remnant of hypogastric artery, and peritoneal relations of bladder.

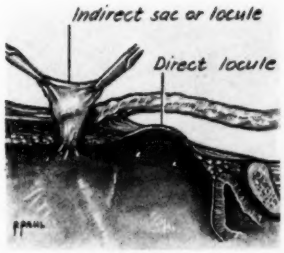

Fig. 2. Same type of section through inguinal canal in case of a bilocular hernia (hernia with indirect sac and direct sac). Notice the peritoneal relationship and anatomical position of each sac with reference to the deep epigastric vessels.

a different entity (Fig. 3). These diverticula do not possess a peritoneal lining or sac. True hernias, not even excluding sliding hernias, always present some sort of peritoneal sac; otherwise they are considered pseudohernias. Routine bidigital palpation of the anterior and posterior surfaces of the inguinal floor will demonstrate more frequently than reported the presence of this type of anomaly. Pseudohernial fatty masses occur most frequently in the indirect position in the vicinity of the internal ring and before operation they are hard to differentiate from indirect hernial protrusions. The importance of this last type of pseudohernial defect mentioned is great. Their presence does not incapacitate patient in any way and rarely produces symptoms. However, with the strictness of industrial laws and industrial physical examinations an individual with this type of defect can hardly obtain employment as he is consistently refused employment because of the presence of an inguinal bulging. The correction and excision of these two common pseudohernial defects are simple enough and, if present, should be routinely corrected through the usual established methods. In our experience we have had instances of patients operated upon in whom these types of defects were encountered at the time of operation and before operation had been mistaken for simple hernias or recurrences, if there was evidence of prior surgical intervention.

The surgical method of repair of inguinal hernias to be described has been steadfastly followed by us in the last 3 years or more and at present a follow-up statistical report is in preparation. This method, with few variations, can be applied to all types of hernial defects encountered in the inguinal regions excepting the double and triple recurrent hernias which almost always bring out, as a rule, other problems of structural weaknesses and have to be met in a different manner by the use of viable fascial sutures or grafts to re-enforce the weakened areas or to create a structure which through some congenital maldevelopment has never been present (10, 11, 18). For instance, in very rare occasions the fascia transversalis has been hard to demonstrate or has been absent and then we have been forced to use a pedicle fascia lata graft. This has been done successfully in few cases. The technique described takes longer than the average method of repair of hernias because of the complete and meticulous dissection and excision of the peritoneal locules from their attachment to the understructure of the floor of the canal and lateral bladder wall. On this dissection, we insist, as the radical removal not only of the indirect sac but also of all associated direct sacs or locules is of prime importance, and we believe it bears a definite relation to the success or failure of any inguinal herniorrhaphy. Recurrent hernias are frequently of the direct variety, the indirect sac having been properly excised at the time of the original repair.

Bassini (6) advocated the radical removal of the indirect sac down to its neck and following his

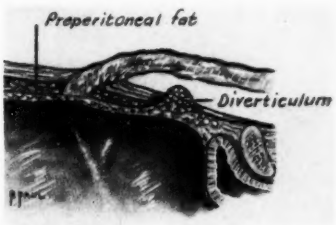

Fig. 3. Same type of section through inguinal region in which there is a diverticulum. Notice peritoneal relation to this diverticulum. This is a pseudohernia.

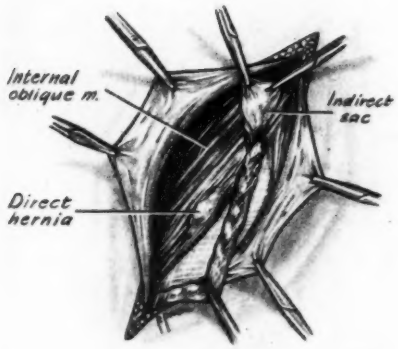

Fig. 4. Appearance of inguinal region after cord has been properly mobilized, presenting an indirect hernia and a direct protrusion.

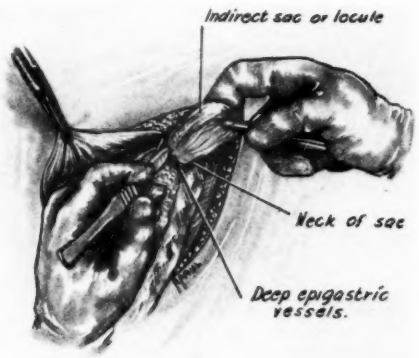

Fig. 5. Indirect sac has been mobilized from the cord and dissection of direct locule is begun. Notice the deep epigastric vessels.

method he obtained relatively brilliant results as compared with the Czerny method which disregarded altogether the excision of the peritoneal sacs and which was, as a rule, followed by more than 80 per cent recurrences. Statistics and our experience reveal that recurrent hernias in the inguinal regions are chiefly of the direct type and we attribute this to failure of removal of the direct sacs at the initial operation although the indirect sac had been properly excised (8). Similarly we have found that our method obviates the more frequent use of other radical methods such as fascial strips or massive fascia lata grafts (9, 10, 11, 18). In very few instances severe structural weakness of such magnitude has been found that fascial grafts of some sort or another have been definitely indicated and successfully used. Lately (19) the reports of the results of fascial sutures or grafts have been discouraging but we believe the fault lies not in the grafts or sutures used but in the improper selection of the cases and in the lack of proper evaluation of the anatomical structural weakness found by the operator. In marked structural weakness of the tissues composing the floor of the canal, particularly of the fascia transversalis, the fascial strips or sutures are of greatest value in correcting the defects present.

It is our purpose to emphasize certain points in the technique described because they are forgotten, misinterpreted, or misapplied in the proper physiological corrections of hernial defects in the inguinal regions with the subsequent failures and recurrences. First, the inguinal floor presents variations in structural contour which are too many to discuss in this short article. We refer the readers to a recent paper by Anson and McVay in which these variations are described and the frequent areas of structural weakness are pointed out and discussed. At the time of operation when the floor is exposed it should be thoroughly inspected and studied to the end that the weak areas discovered be properly taken care of later in the process of reconstruction of the wall. The fallacy of the conjoined tendon as an unfailing strong pillar that can be used as the main axis in the proper repair of the floor of the inguinal canal is clearly brought out and dispelled by the workers quoted. These workers as well as Andrews and Seelig (1, 2, 17), have brought out that the weakness of the floor of the inguinal canal is frequently found in its medial aspect designated by Andrews as the inguinal triangle. Second, the internal oblique muscle fibers found in the inguinal canal are part of the roof of the canal, and their use in rebuilding the floor by suturing them to Poupart's ligament is considered unphysiological. The muscle will not remain strongly attached at the place where it is sutured as union takes place only between the connective tissues of the muscle fibers, the epimysium, and the ligament. The union of muscle fibers is relatively stronger in tensile strength than the union of muscle to fascia or white connective tissue. Therefore it is essential that like tissues be placed in contact in order to obtain the strongest and most sturdy physiological final fusion in the repair. Third, the application of tension in bringing tissues together should be avoided. The use of relatively strong fine silk sutures is the ideal inasmuch as these are

of sufficient strength to hold the approximated tissues together, and are weak enough to break in case unnecessary tension is made. Fourth, after the indirect sac is opened a thorough digital examination of the under surface of the floor should be done to help in correlating the facts observed in the study of the floor anteriorly. Fifth, the complete removal of all peritoneal sacs in the direct and indirect positions is of paramount importance. The dissection of the direct locule or locules takes little additional time and the danger of opening or damaging the urinary bladder is negligible if proper care is used. If the bladder wall is accidentally opened, it should be immediately repaired by suturing the rent. If there is no complicating cystitis or urinary infection, no drainage of the operative wound is indicated and as a rule healing of tissues takes place by primary intention. The insertion of an indwelling catheter in the bladder for 48 hours is very desirable following an accident like this. In our series of cases in 2 instances the urinary bladder was accidentally opened and immediately closed, both patients making an uneventful recovery, the wounds healing by primary intention. As a rule, after complete dissection of the sacs and converting them into one, it is possible to twist the peritoneal sac and easily insert a purse-string suture at its base. The stump left after amputation of the excess sac, if this has been properly dissected, retracts backward and upward for an inch or more.

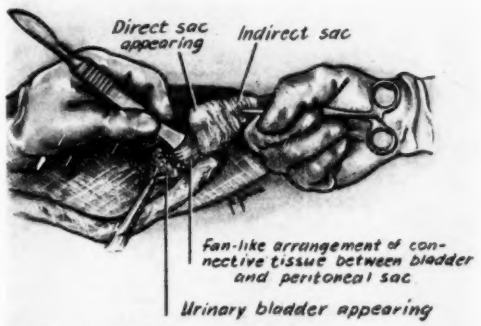
Direct sac appearing
Indirect sac
Fan-like arrangement of connective tissue between bladder and peritoneal sac
Urinary bladder appearing

Fig. 6. Dissection has progressed. All direct sacs or locules have been dissected free. Notice the fan-like arrangement of peritoneum and bladder wall at this stage.

TECHNIQUE

The steps of the operation are illustrated in Figures 4 to 9. The usual incision for inguinal hernia is made, exposing the aponeurosis of the external oblique muscle which is incised over the middle of the canal down to the external ring and reflected from its muscle attachment. The cord is grasped, taped, and mobilized, excising the excess cremasteric fibers. The floor of the canal is then found to be clearly delineated and its weak areas and defects are observed (Fig. 4). The indirect locule is identified, dissected sharply and bluntly from its attachment to the cord and under brim of internal muscular ring. The sac is opened and any adherent viscus or omentum to its inner surface is released. One or two fingers, depending on its size, is introduced into the sac and palpation of the under surface of the floor is done, thus supplementing the observations made by external inspection. Gently the indirect sac is pulled upward and laterally (Fig. 5), exposing the deep epigastric vessels and preperitoneal adipose layer which are dissected and displaced medially. This is done with the idea of "indirectilizing" all sacs of the direct variety present; that is, changing the direct locules into the indirect position, anatomically speaking. The remnants of the embryonic hypogastric artery (lateral umbilical ligament) appear as the dissection continues medially and the edge of the urinary bladder is encountered a few centimeters beyond this embryonic structure. The bladder wall is held taut with a hemostatic forceps by the assistant who exerts slight traction medially and upward, exposing a sort of fan-like arrangement of the areolar tissues between the peritoneal sac and bladder wall (Fig. 6). The peritoneum is further dissected from the bladder wall and soon it is found that there is no convexity but just a straight peritoneal fold extending downward and backward. By following the lines of cleavage between the bladder wall and peritoneum and by exercising gentleness, tearing through the sac is seldom and the bleeding negligible. The sac is then twisted and its base is pursed with a doubled fine silk suture. The sac is excised, the stump as a rule retracting approximately one inch. We are opposed to transfixion of the stump of the sac as to do this is to admit the inadequate removal of the sac. The only exception is in sliding hernias in which the complete mobilization of the sac is not possible without compromising the blood supply of the attached bowel. In rebuilding the floor of the canal the muscle fibers of the internal oblique and transversus are retracted exposing the underlying fascia transversalis (Fig. 7).

Seelig (16) has pointed out his difficulty in identifying the fascia of the transversus at times, and we occasionally have had similar experiences. The first suture with fine black silk rebuilds the internal ring proper by bringing the muscle fibers

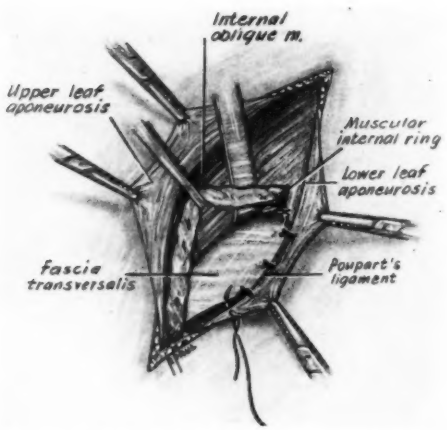

Fig. 7. First stage of repair. Fascia transversalis has been attached to Poupart's ligament. Notice the first suture next to the cord which is muscular. This is the first fascial floor mentioned in operation. Internal oblique muscle is retracted.

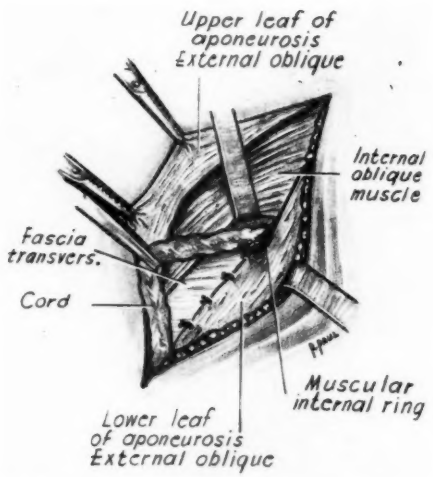

Fig. 8. Second stage of the repair. The lower aponeurotic flap has been tacked on the fascia transversalis. This is the second fascial floor. The muscle is still retracted.

of the transversus and oblique muscles to a shelf of these same muscle fibers which are always found attached to the undershelf of Poupart's ligament just caudal to the outlet of the cord (Fig. 7). At this stage, if there is a dome-like relaxation of the fascia transversalis in the inguinal triangle or true diverticulum, this is cleaned, a purse-string suture is inserted and inverted, as suggested by Andrews and Bissell (3). Continuing with interrupted fine black silk sutures the fascia transversalis is brought without tension to the shelving edge of Poupart's ligament, thus creating the first fascial layer of the floor in reconstruction. Then the lateral or outer leaf of the aponeurosis of the external oblique is attached with the same type of sutures to the upper surface of the fascia transversalis, allowing sufficient space so that the cord is not constricted or kinked, thus forming the second fascial layer of the new floor (Fig. 8). The retracted internal oblique muscle is allowed to fall in place and the medial leaf of the aponeurosis is tacked down to the lower leaf, thus making the third fascial layer of the floor of the canal (Fig. 9). Above the internal ring the edges of the aponeurotic leaves are approximated with a few interrupted sutures. A new floor has been created which is structurally strong and of sufficient resiliency to withstand any stress placed upon it from within. The cord is dropped in its new bed and the fatty subcutaneous layer and skin are closed in the usual manner. The cord as it will be noticed assumes finally an extra-aponeurotic position.

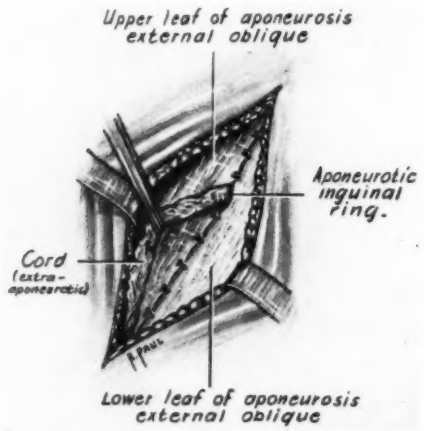
Upper leaf of aponeurosis external oblique
Aponeurotic inguinal ring.
Cord (extra-aponeurotic)
Lower leaf of aponeurosis external oblique

Fig. 9. Last stage of the operation. The oblique muscle has been allowed to fall in normal place. The upper aponeurotic leaf has been attached to the lower aponeurotic leaf, creating a third fascial layer of the newly reconstructed floor. The cord finally is placed extra-aponeurotically.

UNUSUAL ANATOMICAL VARIATIONS

If there is a large femoral ring, the fascia transversalis should be attached to Cooper's ligament instead of the shelving edge of Poupart's ligament following the technique described by Dickson. In

a few cases in which weakness or incompleteness of the floor is still present after attaching the fascia transversalis to Poupart's ligament due to frailness, severe relaxation, attenuation or absence of the fascia transversalis, then the use of strips of fascia lata may be advantageously used to re-enforce and correct the weak area (1, 10, 11). This procedure takes but a few minutes with the help of a Grace or Maxson's fascial stripper. In very large defects the use of fascial pedicle graft is obvious and the procedure of choice is that described by Wangensteen (18). One of us has been quite successful in using the femoral canal for the passage of the mobilized iliotibial tract pedicle graft. This type of graft as a rule is sutured to the under surface of the rectus muscle, thus replacing or re-enforcing the fascia transversalis. The Kirschner fascial patch graft does not produce as strong and resistant a wall, in our opinion and experience, as does the fascial pedicle graft.

SUMMARY AND CONCLUSIONS

1. The complete removal of the peritoneal sac with all its locules, the approximation of like tissues which have been properly mobilized to avoid tension, are considered of paramount importance in the successful repair of hernias.

2. The usual operations for indirect hernias are considered inadequate, as is indicated by the frequency of recurrences, mainly because of the incomplete eradication of the direct locule or locules of peritoneal sacs present and because of the unphysiological repairs made by the approximation of tissues which histologically and physiologically are different.

3. A single flexible surgical method of repair of inguinal hernias has been described, which is applicable to all types of defects in the inguinal regions not excluding the recurrent hernias. The rare variations necessary at times are described in the body of the article.

4. The occurrence of simple, indirect hernias (monolocular) is relatively rare after the age of 30 years.

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A SAFE SURGICAL SPONGE

EDWARD F. LEWISON, M.D., New York, New York

THE loss of a surgical sponge is a most deplorable accident. Yet the medical literature has shown an almost complete indifference toward this operative catastrophe. The development of operating room procedures to contend with this problem has been, for the most part, a measure of prophylaxis. The "sponge count," the use of "stick sponges," the metal-clipped or ringed laparotomy pads, the wire-threaded sponge, the "sponges on a string," and the continuous sponge are all important precautions primarily designed to prevent the losing of a surgical sponge. The meticulous regard with which the surgeon and his assistants are trained to convoy each free piece of gauze placed within the operative field is a tribute to the care and caution needed to preclude the possible inclusion of a tampon within the incisional closure. Despite these measures, some of which are inadequate and objectionable and others cumbersome, "lost" surgical sponges and laparotomy pads remain a rare but corrigible cause of grief after operation.

The problem of the missing sponge will continue to be a surgical hazard, regardless of the virtues of the many present plans of prophylaxis, as long as individual sponges are so used. Fundamentally, the safeness of a "lost" surgical sponge must exist in the ease and manner of its redemption and the facility with which it can be rapidly recognized, localized, and readily retrieved.

Interest in this problem was stimulated several years ago when a patient was admitted to the Johns Hopkins Hospital with a persistently draining sinus 1 year after an appendectomy. The diagnostic possibility of the presence of a gauze foreign body was naturally pre-eminent, yet the hazards of an operative exploration were considerable, thus making the problem a difficult one.

Of approximately 27,250 abdominal operations performed at the Mayo Clinic[1] over a 5 year period, 13 were for the removal of a gauze foreign body. As statistical accuracy is rather difficult to obtain, it may be reasonably assumed that a certain number of retained sponges may be compatible with good health, and similarly a certain number responsible for early death after operation.

These and similar experiences have prompted this investigation for a reliably redeemable surgical sponge. The character and extent of this research have resulted in the experimental use of all the known radio-opaque substances in the hope of producing a safe surgical sponge which might be readily detected on an x-ray film. Inasmuch as ordinary cotton gauze casts no x-ray shadow, it was not until the recent advent of glass fiber in the manufacture of fabrics that a practical and satisfactory solution to this problem was found. By incorporating into the gauze mesh a single strand of glass thread specially prepared with a predetermined lead content, a surgical sponge harmlessly inert and of marked radio-opacity was produced. Whether the introduction of lead glass thread will have an even more extensive use in the future field of surgery is at present difficult to say. However, further study along such lines is now in progress.

MATERIALS AND METHODS

Thus, with the objective well in mind—that of finding a safe and satisfactory tampon that would cast a permanent x-ray shadow—a systematic search to investigate each of the many well known radio-opaque contrast media was begun. Attention was first directed to the iodides because of their relatively high radio-opacity and the frequency with which they are so employed. Several small squares of sterile gauze mesh were first immersed in solutions of sodium iodide of various strengths, namely, 7½, 15, 25, 50 per cent, and a saturated solution. These squares were carefully sutured in sequence to the parietal peritoneum of a dog and x-ray films were taken at weekly intervals to determine the opacity of the shadows cast. It was found that all shadows disappeared in a period of 4 weeks, and the time of disappearance varied directly with the strength of the solution used. The factors responsible for this loss of radio-opacity in so short a span of time are speculative. However, it may be assumed that the sodium iodide entered into solution with the surrounding body fluids and was rapidly diffused throughout the body.

From the Division of Surgery, Northwestern Medical School and Passavant Memorial Hospital, and the Department of Pathology, Johns Hopkins Hospital.

Dr. Lewison was located formerly in Chicago.

[1] MASSON, J. C. An extra tag on the abdominal sponge. J. Am. M. Ass., 1919, 72:22.

Fig. 1.

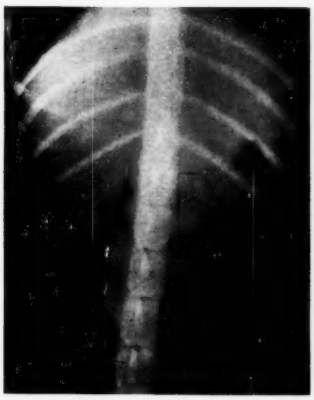

Fig. 2.

Fig. 3.

Fig. 1. Film taken February, 1938, 1 month after placing a lead glass-threaded sponge within the peritoneal cavity of a dog. The arrow points to the single strand of lead glass fiber in the left upper quadrant. The gauze mesh of the sponge casts no x-ray shadow.

Fig. 2. Film taken May, 1938, 4 months after placing the sponge. The arrow points to the lead glass fiber.

Fig. 3. Film taken September, 1938, 8 months after placing the sponge. The arrow again points to the lead glass fiber. The 2 additional strands of lead glass thread which are visible in this film are being used to determine tissue reaction.

Further studies of a similar nature, making use of barium, bismuth, thorium, iodized oils, and lead-weighted silk, in a series of 4 experiments using 2 dogs, were made but with disappointing results. Characteristics of the undesirable effects of these materials were: (1) rapid loss of radio-opacity; (2) marked tissue reaction; (3) loss of absorption quality of the gauze mesh; and (4) difficulties relating to the physical properties of the contrast media used. These serious objections were sufficient to make their use inadvisable.

As previously mentioned, the recently extended use of glass thread, made by forcing potassium silicate through many minute holes with high pressure steam jets in the field of textiles, has given added zest to the successful solution of this problem. Sample fibers of glass thread were obtained for experimental study. Ordinary glass thread, however, cast no x-ray shadow, yet it seemed that this material was admirably well suited for its intended purpose. Its pliancy, delicacy, and high tensile strength, in addition to its

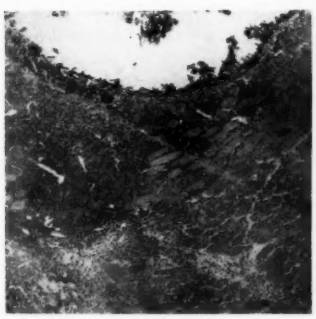

Fig. 4.

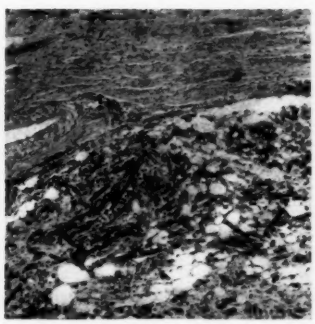

Fig. 5.

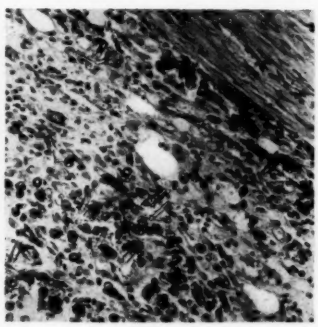

Fig. 6.

Fig. 4. Section of rectus muscle 48 hours after implanting a large thread of lead glass fiber. Oval space at top of section represents site at which thread was placed. Moderate leucocytic tissue reaction. ×80.

Fig. 5. Section of subcutaneous tissue 1 month after implanting a thread of lead glass fiber. Low-grade tissue reaction; marked connective tissue proliferation. ×190.

Fig. 6. High power magnification of section shown in Figure 5. Characteristic mononuclear cellular response. Fibroblastic activity indicates reparatory process. ×400.

Fig. 7. Roentgenogram of the right upper quadrant of an obese female. The lead glass thread is clearly defined between a gall stone and residual barium in the large bowel.

negligible cost of production, were factors of considerable importance. Further study found it possible to alter the chemical composition of the glass thread. By the addition of lead to the potash silicate, a strand of glass thread could be produced of such radio-opacity that the x-ray shadow cast was of a density equal to that of bone. It was then feasible to interweave a single strand of this lead glass thread, composed of innumerable minute fibers .0002 of an inch in diameter, into a small square of gauze mesh and place it within the abdominal cavity of an experimental animal. X-ray films were taken at bi-weekly and then monthly intervals over a period of 8 months to determine its permanence and opacity.

After 1 month (Fig. 1) the x-ray film showed clearly the presence of the lead glass-threaded sponge in the upper left quadrant of the dog's abdomen. Four months later (Fig. 2) the film revealed no appreciable change in the thread's radio-opacity, and from the shadow cast it could hardly be confused with any other structure in the body. At the end of 8 months a lateral film (Fig. 3) again confirmed the permanence of the opaque shadow and gave no evidence of its possible loss of contrast density. This gave rather conclusive proof that radio-opaque lead glass thread retained a remarkable longevity and could be used expediently in this capacity, should its other properties prove desirable.

The 2 additional strands of lead glass thread that strikingly stand out in Figure 3 were placed within the abdominal wall to determine the tissue reaction of this thread. Blocks of rectus muscle and subcutaneous tissue were resected at intervals of 1, 2, 7, 14, 30, and 240 days. A section through the rectus muscle (Fig. 4), 2 days after implanting a heavy piece of lead glass thread, reveals only a moderate leucocytic infiltration in the adjacent muscle. The tissue reaction seems well localized and no greater, considering the incident trauma, than that stirred up by catgut of a similar size. Glass thread, like glass, is a relatively inert substance and would be expected to cause a minimum amount of tissue reaction. After 30 days (Figs. 5 and 6) a section of abdominal subcutaneous tissue clearly illustrates the glass thread, fragmented in the preparation of the section, and the low-grade mononuclear cell infiltration that is present. New connective tissue proliferation is conspicuous and is an important part of the animal's reparatory process.

Figure 7 represents the radio-opacity of a lead glass-threaded sponge when filmed through the tissues of an obese female. The thread is clearly defined when contrasted with the opacity of a gall stone above and residual barium in the large bowel below.

SUMMARY

The "lost" surgical sponge is frequently a disastrous mishap. Because the present methods of sponge control are only partially satisfactory, this investigation was undertaken in the hope of providing a readily recognizable safe gauze tampon. All of the commonly known radio-opaque materials were exploited to this end and none found to be practically expedient. A specially prepared product, namely, lead glass thread, was found to embody these qualities: marked radio-opacity, permanent radio-opacity, minimum tissue reaction, negligible cost of production, chemical inertness, pliancy, delicacy, and appearance resembling white silk thread. As a result a single strand of lead glass thread may be interwoven in surgical gauze mesh and the *presence* and *location* of the "lost" sponge determined with facility.

Mr. H. P. Hood and Mr. G. V. McCauley, Corning Glass Co., were most helpful in preparation of lead glass thread.

EDITORIALS

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HARVEY CUSHING

THE Editors of SURGERY, GYNECOLOGY AND OBSTETRICS join the surgical world in sorrow over the death of Harvey Cushing. As a stimulating investigator both in the laboratory and at the bedside, he had the ability to record his experiences in a fascinating style which made him equally famous as an author as a surgeon and scientist. No other single individual in recent years has exerted such a profound influence upon the art of surgery.

UNUNITED FRACTURES OF NECK OF FEMUR

NON-UNION of central or intracapsular fractures of the neck of the femur is of frequent occurrence, despite the universal accessibility of modern roentgenographic equipment and improved methods of surgical treatment. Because of the mechanical and physiological status of this region, non-union may be expected in approximately 10 per cent of cases, regardless of the efficiency of the treatment employed. The majority of ununited fractures at this point, however, arise from failure to make a diagnosis and from inefficient treatment. Since the revival and improvement of internal fixation, the proportion of successful results has been materially increased, but these procedures are still too often inaccurately applied by those who have not mastered the operative technique.

Non-union is reached much sooner in fractures of the neck of the femur than in fractures elsewhere. When reduction is not accomplished early, there is a wide separation of the fragments and, from a practical point of view, non-union is present at the end of four weeks. Union has been induced by reduction alone after the elapse of three months, though such a result is exceedingly rare.

Until recent years non-union was a hopeless condition; now, however, a large percentage of patients can be assured a useful extremity with partial or complete restoration of function by operative measures. The object of all operations for ununited fractures of the neck of the femur is restoration of an osseous support for the upper extremity of the femur and elimination of shearing action at the site of fracture. This is accomplished by two methods: first, by inducing union at the fracture site, when feasible, and, second, by some reconstructive measure which will place the lower extremity directly beneath the pelvis, to provide an osseous support for weight bearing on the longitudinal axis of the femur. The surgical procedures employed for these purposes are as follows: (1) internal fixation by metal, (2) internal fixation by metal and bone

graft, (3) internal fixation by bone graft, (4) reconstruction operations, (5) osteotomies.

Internal fixation by the first three methods is designed to secure union at the point of fracture. The technique of these procedures is well known. The earlier the operation is undertaken, the greater the likelihood of excellent functional and anatomical results.

The reconstruction operations consist of the remodeling of the upper extremity of the distal fragment, with or without removal of the head of the femur, and restoration of the leverage action of the abductor muscles. By the Brackett operation, the upper extremity of the distal fragment is remodeled, the greater trochanter removed, and the lower fragment displaced inward to approximate the head; the trochanter, with the abductor muscles intact, is fixed to the lateral surface of the shaft of the femur at a lower level. The Whitman reconstruction differs from this only in that the head is excised and the remodeled upper extremity of the lower fragment is placed within the acetabulum. Colonna excises the head, severs the tendons of the abductor muscles, places the trochanter with its tendinous investment within the acetabulum, and inserts the detached muscles at a lower level on the femoral shaft. Albee excises the head, performs a longitudinal osteotomy of the upper extremity of the femur, displaces the fragment with the greater trochanter outward, and inserts a wedge graft, usually the head of the femur, into the space thus created, to maintain the bone-muscle lever in a lateral position.

The osteotomies are of two types: the high, and the low or Schanz. In the high osteotomy, the femur is severed in the region of the lesser trochanter and the lower fragment is displaced beneath the head of the femur and across the line of fracture, as a living graft. The extremity is then immobilized in abduction, thus producing an angle between the two fragments. By this procedure, shearing action is eliminated and union is often induced at the point of fracture, with restoration of almost normal function. Otherwise, the upper extremity of the lower fragment approximates and receives osseous support from the pelvis, which usually gives a fairly serviceable member. The low, or Schanz, osteotomy is carried out at the level of the tuberosity of the ischium, and the lower fragment is abducted to induce inward angulation; the upper fragment is supported by the lateral aspect of the pelvis, eliminating shearing force at the site of non-union. The chief objection to this measure is the fact that undue strain is placed on the internal lateral ligament of the knee, which in some cases leads to genu valgum deformity.

The indication for these procedures varies according to the age and physical condition of the patient and the local status of the fracture. Operations undertaken soon after non-union is established offer a much better prospect of a functional hip, since, with the passage of time, the fragments undergo atrophic changes and the neck is gradually absorbed. If operation is delayed, therefore, the possibility of restoring normal anatomical relationships is commensurately decreased. The non-viability of the head cannot be accurately determined from the roentgenographic demonstration of an increased density of the head alone, unless the structure is practically opaque. The head is normally dense and does not undergo atrophic changes so rapidly as the surrounding bone; further, if the head is atrophic prior to fracture, there will be little or no contrast between the head and the adjacent bones.

Restoration of anatomical contour is of course desirable. If the structure of the bone is good and the head viable, internal fixation as of fresh fractures is advisable and frequently can be accomplished by blind nailing. This

procedure may be employed in many cases until the elapse of approximately three months. After atrophic changes and pseudo-arthrosis are established, the insertion of a bone graft, with or without metallic fixation, is preferable. This often requires exposure and denudation of the ends of the fragments. In the presence of extensive atrophic changes, internal fixation of any type must be followed by immobilization in plaster casts and braces for a period of six to twelve months. Such prolonged immobilization not only is a physical handicap, but also may impose a serious financial burden upon the patient. If his economic status will permit and his physical condition is good, anatomical conformity and practically normal function may be anticipated. Other procedures, however, which do not require such long confinement, give results which compare favorably with those of internal fixation.

Reconstruction operations, with the exception of the Brackett reconstruction, are employed only in the presence of extensive atrophic changes in the bone or a non-viable femoral head, with or without absorption of the neck. These procedures are followed by failure in a large number of cases, and even when successful, the functional results do not equal those obtained by internal fixation or osteotomy. The Brackett operation is not advisable if the head has undergone aseptic necrosis.

High osteotomy is especially indicated in the aged and debilitated if absorption of the neck is not extensive; osseous union may often be induced, with excellent function. Even if union fails to take place, a support is provided which permits weight bearing without crutches and gives a result comparable to that of a reconstruction operation. The low, or Schanz, osteotomy is most suitable when absorption of the neck is extensive and the head necrotic, or when reconstruction operations have failed. Osteotomies are particularly advantageous in that they cause less surgical shock than any other procedure and, with the exception of that incident to early internal fixation, the period of confinement is shorter.

In conclusion, the most important factor in the treatment of ununited fractures of the neck of the femur is the determination of the state of non-union as early as possible, since the sooner operative measures are instituted, the more successful the outcome. When feasible, internal fixation by metal or by bone graft, and high osteotomy, give the best functional results. After absorption of the neck or necrosis of the head, reconstruction operations, with or without excision of the head, or low, or Schanz, osteotomies are the procedures of choice. Whatever the local condition, when the measures devised for this purpose are judiciously employed, the prognosis of ununited fractures of the neck of the femur is far more favorable than in the past.

WILLIS C. CAMPBELL.

TOTAL CYSTECTOMY FOR CARCINOMA OF THE BLADDER

FROM the points of view of maintenance of normal physiological functions, choice of therapeutic procedure, operative risk, and likelihood of ultimate cure, the management of carcinoma of the bladder presents many more problems than the treatment of carcinoma in most other parts of the body. In contrast with carcinoma of the breast, kidney, uterus, and many other organs, wherein the indications for treatment and method of attack are relatively standardized and widely accepted, each case of carcinoma of the bladder presents a distinctly individual therapeutic problem. Not only must the function of the bladder be preserved or some suitable provision made if the bladder

is removed entirely, but even more important is preservation of renal function and the prevention of serious renal infection.

Choice of the ideal therapeutic procedure for the individual patient who has a vesical neoplasm depends on a number of factors: the type, grade of malignancy, extent and exact location of the lesion; whether the ureterovesical orifice on one or both sides has been encroached on; the status of renal function; the presence or absence of important renal infection; and, of great importance, the age and general condition of the patient. Obviously when so many factors must be considered, almost all of which are necessarily dependent on personal interpretation for their relative evaluation, there is ample opportunity for difference of opinion regarding the choice of therapeutic procedure. This fact, together with the numerous methods of treatment which are available in the management of carcinoma of the bladder, have added to the difficulty of standardizing forms of treatment and evaluating end-results obtained by various procedures. The mature, clinical judgment which is necessary in selecting the most desirable type of treatment must be learned largely by experience. Gradually during the last 25 years, as the many problems involved have become more clearly appreciated, certain facts and general principles in the treatment of vesical carcinoma have evolved. During this period experience with total cystectomy has grown, but the exact indications, most desirable method of execution, and results that might be anticipated in a large series of well selected cases, remain to be accurately determined. That complete removal of the bladder has a definite place in the management of vesical carcinoma, however, cannot be denied.

The indications for total cystectomy have undergone a gradual change during recent years. In the past this procedure was almost uniformly reserved for the advanced, extensive, high-grade lesion, possibly recurrent in nature, which could not possibly be treated with any expectation of cure by less radical measures. In cases of this type, extension of the lesion beyond the confines of the bladder and even distant metastatic growths were undoubtedly often present, although perhaps unappreciated, at the time when the bladder was removed. Under these circumstances satisfactory results were not obtained and could not be expected, and consequently the operation failed to gain wide favor. At the present time it is believed that total cystectomy has a different field of usefulness and is frequently contra-indicated in the type of case just mentioned. One does not have justification for the performance of so extensive a staged procedure without reasonable hope of ultimate cure.

It is now realized that an extensive, relatively low-grade carcinoma, too large to be dealt with satisfactorily by transurethral measures, and which would require for its adequate removal almost complete resection of the bladder by the suprapubic approach, probably constitutes one of the ideal indications for total cystectomy. Likewise a repeatedly recurring low-grade lesion which has resisted conservative forms of treatment, or one which apparently has multiple foci of origin, comparable to the extensive carcinomatosis sometimes seen in association with polyposis of the colon, may offer a suitable indication for total extirpation of the bladder. The high-grade, infiltrating type of lesion which, to the best of one's knowledge has not progressed beyond the bladder, may best be treated in this same manner. In addition to these types of cases in which the indications for total cystectomy may appear to be fairly definite, there are other cases in which, in the judgment

of the individual surgeon, complete removal of the bladder may be considered the treatment of choice.

The general plan of procedure in the performance of total cystectomy will vary depending on the exact findings in the individual case and the experience of the surgeon. It is now well recognized that the risk of operation is definitely higher when grossly dilated and otherwise abnormal ureters are transplanted into the bowel. In general, ureterosigmoidal transplantation is wisely reserved for the ureter of normal or relatively normal size, although exceptions may be made. In contrast, the risk is lower and the results are better if cutaneous ureterostomy is employed when considerable ureterectasis exists.

Whether total cystectomy is best accomplished in one, two, or three stages will depend on the conditions found in the individual case, on the type of ureteral transplantation that is contemplated, and on the surgeon who is performing the operation. In former years three stages were commonly employed when ureterosigmoidal anastomoses were established. Each ureter was transplanted separately and subsequently the bladder was removed. In general, three major operations performed on a patient suffering from cancer are not desirable. Simultaneous bilateral ureterosigmoidostomy can be performed in well selected cases with reasonable operative risk. It is the opinion of many that the two-stage procedure, with initial transplantation of both ureters into the bowel, and two or three weeks later removal of the bladder, is usually the best plan of procedure. In contrast, if the ureters are to be transplanted to the skin and if there appears to be urgent need for extirpation of the bladder, the entire operation can be performed in one stage by an experienced surgeon with reasonable risk. A safer plan of procedure for the average surgeon, however, is initial bilateral cutaneous ureterostomy and subsequent removal of the bladder.

It would be only a slight exaggeration to say that there are almost as many methods for performing ureterosigmoidal anastomosis as there are surgeons who perform this operation. Because of this fact the technical procedures involved in the transplantation of the ureters into the bowel will not be discussed. The essential features which all endeavor to embody in their own particular operation are: asepsis; and lack of tension, angulation, or obstruction, either temporary or permanent, where the ureter traverses the wall of the bowel. Appropriate pre-operative and postoperative care is essential for the best results.

It has been implied that the patient who has undergone total cystectomy is not in condition to lead a normal and useful life. This implication can be definitely and truthfully denied. Transplantation of the ureters into the bowel works little hardship on the patient and is not at all incompatible with a normal, active life. Control of the bowel content is satisfactory, provided that the rectal sphincter functions normally. In addition, the patient may be spared repeated cystoscopic examinations and other procedures which are often necessary during a prolonged period of years (if he survives) following less extensive forms of treatment. Cutaneous ureterostomy, it is true, does not create an ideal state of affairs, but is comparable in its disagreeable features to colostomy, which has been an accepted operation for many years. When possible, of course, transplantation of the ureters to the bowel rather than transplantation to the skin is to be desired.

JAMES T. PRIESTLEY.

CORRESPONDENCE

PROFESSOR ARCHIBALD YOUNG

1874–1939

AMERICAN surgery, on July 23, 1939, lost a dear friend and an eminent colleague in the death of Archibald Young, regius professor of surgery at the University of Glasgow. Professor Young was born in Glasgow and went through all his schooling in that vicinity. He graduated from the University of Glasgow with distinction and following this went through a long period of hospital training, finishing as senior assistant to Sir William Macewen who then held the chair which Professor Young himself was later to decorate.

Archibald Young was embued with a high ambition and followed the finest ideals of surgery. He was a most industrious person. When he achieved his appointment in 1924 as regius professor of surgery at the University of Glasgow he set about to maintain for the Glasgow school that eminent place in surgery which it had held from the days of Lister and which had been visioned ever since Peter Lowe returned from France and founded the Faculty of Physicians and Surgeons of Glasgow. Dr. Young busied himself in many fields, including the operative treatment of fractures, skin grafting, peptic ulcer, and for several years before his death he made special contributions to the field of the surgery of the sympathetic nervous system.

He not merely was a teacher of surgery but, in addition to serving both in the South African War and in the Great War, was a fine citizen in the City of Glasgow and assumed positions of importance in civilian life.

Professor Young's qualifications led him to acquire great distinction. He became a member of the Royal Academy of Physicians in Rome. He was an honorary fellow of the American Surgical Association, of the American College of Surgeons and of the Academy of Surgery, Philadelphia. He received the degree of Doctor *honoris causa* from the University of Strasbourg and was an honorary member of the Academy of Surgery of France. His ambition was to stimulate the advancement of scientific surgery by the unselfish collaboration of many workers, and all his life he strove to provide the opportunity for useful work to those willing to undertake research.

Professor Young's many friends in America will miss his sincere and stimulating nature and send their sympathy to his widow and two children, one of whom is a young doctor.

ELLIOTT C. CUTLER, M.D.
Boston, Massachusetts

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

IN his introduction to *Chronic Diseases of the Abdomen; a Diagnostic System*,[1] Marshall says, "in this work, which of course does not pretend to be an encyclopedia of abdominal disease, an attempt is made, while omitting no important condition in the diagnostic problem in any given entity, to assess at their real value the observations in history, clinical, laboratory and other special examinations, which may be utilized to arrive at dependable conclusions." In a large measure Marshall has attained this objective. The first 52 pages are devoted to methods of examination. The section dealing with history taking contains some valuable advice. The guide to the general physical examination which Marshall refers to as the "diagnostic net from whose meshes no big pathological fish can escape" is excellent. The last 155 pages deal with differential diagnosis of abdominal conditions considered first from the standpoint of pain, both general and regional, and second from the standpoint of significant symptoms including hematemesis, ascites, variations in appetite, weight loss, jaundice, diarrhea, hematuria, vomiting, and pyrexia. The illustrations are pertinent but only fair in quality.

The book stamps its author as a thoughtful surgeon with wide clinical experience. The reviewer wishes the author had differentiated better the symptomatology of the right and left sides of the colon and regrets the extent of the reference, even guarded as it is, to Glenard's disease. The book cannot fail to be valuable to students and practitioners and stimulating to specialists. FREDERICK CHRISTOPHER.

THE Essentials of Modern Surgery[2] is an English textbook edited by Handfield-Jones and A. E. Porritt with the co-operation of 13 of their colleagues. The authors have attempted to produce a textbook of surgery which will neither be a comprehensive product of two or more volumes, nor a short text in one volume with easily assimilable material with which the student can satisfy the examiner. The purpose of the authors is to put forth a volume in which surgical teaching is based on the fundamentals of anatomy, physiology, and pathology, thereby building a sound foundation upon which the student as well as the practitioner can think for themselves, rather than subject every patient to countless laboratory investigations.

Detailed operative treatment is only rarely included in this book, although the nature of the treatment is well given. The book divides itself into 47 chapters, with 501 illustrations, the latter always exceedingly helpful to the average student and practitioner. Many of the divisions are excellent. "Infections of the Hand and Fingers" is perhaps better stated than in most textbooks in use at our medical schools, and the Kanavel influence can be sensed immediately. The chapter on "Diseases of the Blood Vessels" is especially well handled, while the questions of hernia and appendicitis deserve special commendation. Those interested in "Injuries and Diseases of the Nerves" will find a fine presentation, unlike that found in any textbook of surgery. It is of interest to note that in the discussion of postoperative paralytic ileus, a galaxy of drugs are offered, but no mention is made of the Wangensteen suction method, which to this reviewer is perhaps the greatest adjunct to our armamentarium in fighting this dreadful complication. There is a scholarly dissertation on drainage in peritonitis which should be read not only by medical students but all interested in this much mooted question.

The book is a worthy addition to the many fine textbooks on surgery among which it will find its proper place, but this reviewer can name several American books equally as good if not better.

EARLE I. GREENE.

THE second edition of Dr. Major's book, *Classic Descriptions of Disease*,[3] which has become a standard volume in all medical libraries, contains new sections covering certain diseases not previously described. Dr. Major has collected classic accounts of diseases and has added interesting biographical sketches of each author as well as revising many of those in the previous edition. The text contains numerous interesting and instructive illustrations and should be included in every physician's library.

J. ROSCOE MILLER.

IN a book of 47 chapters Dr. Scudder has organized *The Treatment of Fractures*[4] in a very methodical manner. Measurements of normal and abnormal joint functions are discussed and illustrated. First aid, transportation, and extension are dealt with in a comprehensive manner. Naturally the author is not

[1] CHRONIC DISEASES OF THE ABDOMEN; A DIAGNOSTIC SYSTEM. By C. Jennings Marshall, M.S., M.D. (Lond.), F.R.C.S. (Eng.). Boston: Little Brown & Co., 1939.

[2] THE ESSENTIALS OF MODERN SURGERY. Edited by R. M. Handfield-Jones, M.C., M.S., F.R.C.S., and A. E. Porritt, M.A., M.Ch., F.R.C.S. Baltimore: William Wood & Co., 1938.

[3] CLASSIC DESCRIPTIONS OF DISEASE; WITH BIOGRAPHICAL SKETCHES OF THE AUTHORS. By Ralph H. Major, M.D. 2d ed. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1939.

[4] THE TREATMENT OF FRACTURES. By Charles Locke Scudder, A.B., Ph.B., M.D., F.A.C.S. 11th rev. ed. Philadelphia and London: W. B. Saunders, 1938.

able to go into minute details with each fracture, as volumes could be written rather than chapters; yet the subjects are well covered and important points are stressed.

Fractures from birth injury on have been discussed as to pathology, complications, and methods of treatment. This book is well illustrated with x-ray views, diagrams, and microscopical photographs. The chapter on anesthesia is most commendable and very pertinent especially in view of present day multiple and serious injuries. Spinal injuries with and without cord involvement are of particular interest, though I believe this section could have been discussed a little more extensively, since spinal injuries constitute a very important subject about which little is known and which is worthy of weighty consideration. The chapter on intervertebral disc injuries is stimulating and of paramount importance in view of our inadequate knowledge on this subject. Operative work has been stressed but obviously cannot be extensively discussed or illustrated.

All fractures from the head to the toes have been handled and discussed very well. Each chapter is definitely enlightening in the short space allotted it. I believe that all fractures and their treatment have been either touched upon or emphasized; and while some forms of treatment are controversial, I believe the author has selected the most representative type of treatment for each.

In addition to having all the essentials necessary for a good fracture book, this treatise has a very valuable chapter on the medicolegal relations in fractures supplying a great present day need in view of the fact that most traumatic work entails court appearances. This adjunct completes what, in my opinion, is the best, most practical, and enlightening fracture book of the present day. While I do not agree with all methods of treatment advocated, I must say that there are certain definite, outstanding points in every chapter of this book that should be of great assistance to the student and practitioner.

JAMES J. CALLAHAN.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

OXFORD MEDICAL PUBLICATIONS. PIONEERS IN ACUTE ABDOMINAL SURGERY. By Zachary Cope, B.A., M.D., M.S.(Lond.), F.R.C.S. (Eng.). London: Oxford University Press, 1939.

ILLUSTRATIONS OF REGIONAL ANATOMY. By E. B. Jamieson, M.D. Sections I–VII. 2d ed. Baltimore: The Williams and Wilkins Co. (American distributors), 1939.

CLÍNICA QUIRÚRGICA EN LAS HIDATIDOSIS COSTAL Y PLEURAL. By Pedro D. Curutchet. Buenos Aires, Argentina: Librería y Editorial "El Ateneo," 1939.

MATERNAL CARE AND SOME COMPLICATIONS; THE PRINCIPLES OF ANTEPARTUM, INTRAPARTUM, AND POSTPARTUM CARE AND OF THE MANAGEMENT OF SOME SERIOUS COMPLICATIONS. Approved by The American Committee on Maternal Welfare, Inc. Edited by F. L. Adair, M.D. Chicago: The University of Chicago Press, 1939.

ESGUINCE DE RODILLA. By Dr. Manuel Pérez Zabala. Buenos Aires, Argentina: Sebastián de Amorrortu e Hijos, 1939.

STERILIZATION; A HANDBOOK FOR PHYSICIANS, HOSPITAL EXECUTIVES AND NURSES. By Hurley T. Wyatt, M.S. 2d rev. ed. Madison, Wis.: Scanlan-Morris Co., 1936.

THE RHYTHM; OF STERILITY AND FERTILITY IN WOMEN. By Leo J. Latz, A.B., B.S., M.D., LL.D. 6th rev. ed. Chicago: Latz Foundation, 1939.

PRACTICAL OBSTETRICS. By P. Brooke Bland, M.D., and Thaddeus L. Montgomery, M.D. 3d rev. ed. Philadelphia: F. A. Davis Co., 1939.

THE ROCKEFELLER FOUNDATION. INTERNATIONAL HEALTH DIVISION. ANNUAL REPORT, 1938. New York: The Rockefeller Foundation, 1939.

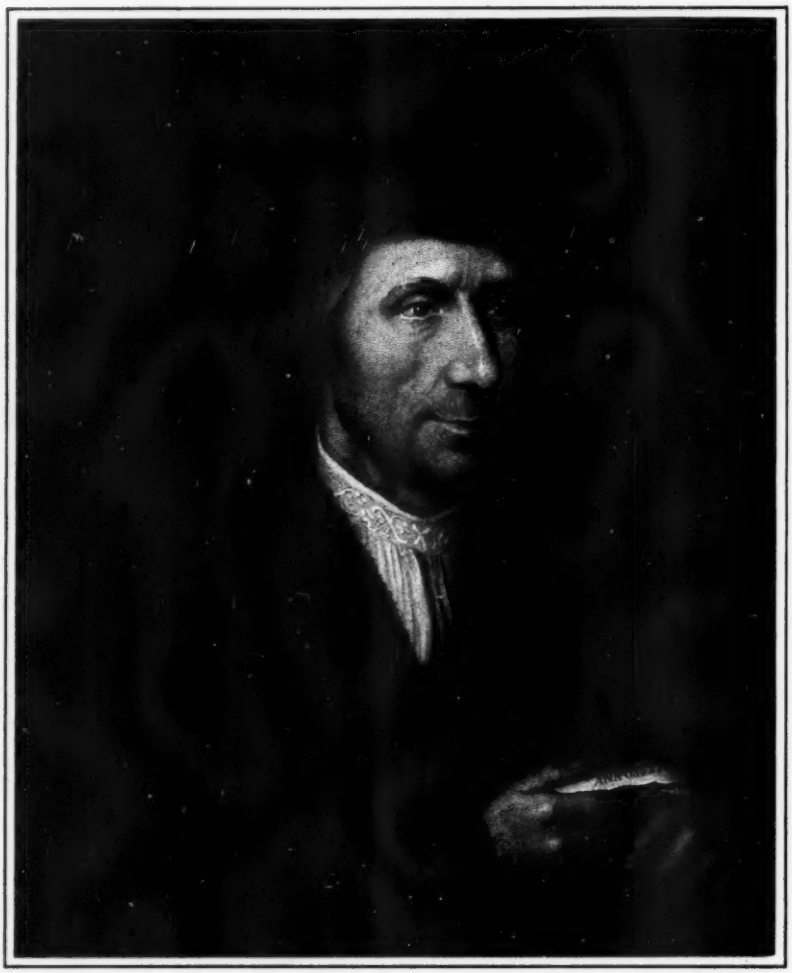
OFFICE GYNECOLOGY. By J. P. Greenhill, B.S., M.D., F.A.C.S. Chicago: The Year Book Publishers, Inc., 1939.

DE PRIMAIRE MAAGRESECTIE BIJ DOORGEBROKEN MAAG-EN DUODENUMZWEREN. By Dr. M. J. Kingma. Assen, Holland: Van Gorcum & Comp. N.V., 1939.

GYNECOLOGIC OPERATIONS; AND THEIR TOPOGRAPHIC-ANATOMIC FUNDAMENTALS. By Prof. Dr. Med. Heinrich Martius. Authorized English translation under editorial supervision of W. A. Newman Dorland, A.M., M.D., F.A.C.S. Chicago: S. B. Debour, Publishers, 1939.

ANESTHESIA; NARCOSIS, LOCAL, REGIONAL, SPINAL. By A. M. Dogliotti, M.D. Authorized English Translation by Carlo S. Scuderi, M.S., M.D., F.A.C.S. Chicago: S. B. Debour, Publishers, 1939.

REGAIN YOUR FIGURE; HOW TO RECOVER THE FIGURE AFTER CHILDBIRTH WITHOUT "STRENGTHENING" EXERCISES. By Lt.-Col. J. K. McConnel, D.S.O., M.C. With a Foreword by Cedric Lane-Roberts, M.S., F.R.C.S., F.C.O.G. Cleveland, Ohio: The Sherwood Press, 1939.



Engraving by H. Cook

Thomas Linacre

1460-1524